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The New England Journal of Medicine

Formerly The Boston Medical and Surgical Journal
Established 1828

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Owned and Published by the Massachusetts Medical Society

Published weekly in Boston at 8 Fenway. Domestic, $6 per annum, 25c per copy; Canada, $7.04; Foreign, $8.52.
Entered as second-class matter, November 16, 1932, at the postoffice at Boston, Mass., under the Act of March 3, 1879.
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The New England
Journal of Medicine

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VOLUME 217 OCTOBER 7, 1937 NUMBER 15

ETHER VERSUS CHLOROFORM

H. E. HOFF, M.D.*

NEW HAVEN, CONNECTICUT

INTRODUCTION

INHALATION of the vapor of sulfuric ether provided the first practicable method of producing insensitivity to pain during surgical operations; its introduction to general use was followed within a few months by the discovery of the anesthetic properties of chloroform. During more than half a century subsequent to this, ether and chloroform remained the only generally successful anesthetics. Each had been introduced in a center of active medical progress, and each found its ardent supporters. The success of chloroform was almost instantaneous, and ether was nearly forgotten, yet today ether has achieved and maintained in most countries of the world an important position as an anesthetic, while the use of chloroform has practically been abandoned.

The story of the fate of these substances subsequent to their discovery, and of the controversy that arose between their partisans, forms an interesting chapter in the history of anesthesia. It has been neglected because of interest in the discovery of anesthesia and in the many problems it involved, and because of the lack of certain essential data; but this material has for some time been available, and it is now possible to give an account of a long and active rivalry—ether versus chloroform.

This story may best be told in two parts. First must be given an account of the reception of chloroform by the surgeons of Boston. Their reactions are significant not only because it was in Boston that ether was introduced to the world, but because through this priority the Boston surgeons possessed the greatest and perhaps the only extensive experience with any other anesthesia when chloroform was introduced, and were thus the only group with a basis for comparison of the newer agent. The broad outlines of this chapter, which becomes essentially a portion of the medical history of Boston, are to be found in the columns of the *Boston Medical and Surgical Journal,* and are supplemented largely by the other writings of Boston anesthetists.

The second chapter of the story deals with the establishment of the scientific basis for the adverse judgment against chloroform, once held only in Boston, but now universally accepted. In this, Boston played a surprisingly small part; on the contrary, it was in England, long a stronghold of the chloroformists, that knowledge of the mechanism of the lethal effect of chloroform was largely unfolded.

BOSTON AND CHLOROFORM

RECEPTION OF ETHER

It may be questioned whether Boston was or was not the scene of the first use of ether as an anesthetic agent in surgery and dentistry, but it is certain that an account of the use of this material was first published there, and it was from Boston that it was disseminated throughout the world. The first notice to appear in a scientific publication was written by H. J. Bigelow,[1] who, in addition to giving an account of its use at the Massachusetts General Hospital, spoke of experiments he had already made with sulfuric ether and chloric ether, with only partial success. In this first report the source of much future trouble was revealed; the nature of the material was secret, and it was to be subject to a patent.

Reaction to this announcement was immediate and energetic. It soon became known that the essential ingredient was sulfuric ether, and use of this substance spread rapidly. No less rapidly, however, there arose violent opposition to its introduction. Typical is that of the profession in Philadelphia, where the influence of Meigs[2] greatly hindered the introduction of any anesthetic. The editor[3] of the *Philadelphia Medical Examiner* wrote:

> We are persuaded that the surgeons of Philadelphia will not be seduced from the high professional path of duty, into the quagmire of quackery by this will-o'-the-wisp; and if any of our respectable dentists should be tempted to try this new *"patent medicine,"* we advise them

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to consider how great must be the influence of an agent over the nervous system to render a person unconscious of pain,—the danger there must necessarily be from such an overpowering medication, and that if a fatal result should happen to one of their patients, what would be the effect on their conscience, their reputation and business, and how the practice would be likely to be viewed by a Philadelphia court and jury? We cannot close these remarks, without again expressing our deep mortification and regret, that the eminent men, who have so long adorned the profession in Boston, should have consented for a moment to set so bad an example to their younger brethren, as we conceive them to have done in this instance. If such things are to be sanctioned by the profession, there is little need of reform conventions, or any other efforts to elevate the professional character—physicians and quacks will soon constitute one fraternity.

The *New Orleans Medical and Surgical Journal*[4] classified the discovery of ether with mesmerism:

That the leading surgeons of Boston could be captured by *such an invention as this,* heralded to the world under the auspices of a *patent right,* and upon *such evidences* of utility and safety as are presented by Dr. Bigelow, excites our amazement. Why, mesmerism, which is repudiated by the *savans* of Boston, has done a thousand times greater wonders, and without any of the dangers here presented. What shall we hear next?

In some local circles opinion was no less antagonistic. Dana[5] complained in reference to an editorial of November 18, 1846:

This attack on mesmerism affords me an opportunity to offer a few remarks upon a subject which has been tested much longer than the inhalation of sulph. ether for producing insensibility during operations, and has been investigated by individuals whose standing as scientific men would not appear unfavorably by the side of members of our own Massachusetts Medical Society.

Even more vehement was the local dentist J. F. Flagg,[6] who on December 2, 1846, wrote concerning Bigelow's report:

But we are still told *it is patented.* What is patented? A power? A principle? A natural effect? The operation of a well-known medicinal agent? I doubt the validity of such letters patent. It would seem to me like *patent sunlight* or *patent moon-shine.*

To my mind it seems unfortunate, to say the least, that the discovery has not been brought to the public notice in a different manner and under different circumstances. And I am sorry that Dr. Bigelow, in his article above mentioned, has attempted to apologize for the arrangements which he says have been made by Dr. C. T. Jackson as one of the parties, to secure by patent the control of a medicinal agent like the one in question.

To patent it would be, what it would have been for the immortal philanthropist Jenner to have patented vaccination.

To this Bigelow[7] replied in an attempt to justify his defense of Morton and Jackson's proposal to patent their discovery, and provoked another outburst from Flagg,[8] who concluded:

Yet at the same time, it is a satisfaction to feel assured, that if the young man had but shown his manuscript to his father, or to any of his seniors in our profession, they would have advised him to have made some different use of it, than that of publishing it in the *Boston Medical and Surgical Journal.*

The general approval of these sentiments is demonstrated by a letter in a subsequent issue of the *Boston Medical and Surgical Journal,* in which Mansfield[9] wrote:

I was much pleased in perusing a paper in your *Journal* of last week, by Dr. Flagg, of Boston, on the inhalation of ethereal vapor in certain cases requiring surgical operations; and I am happy in being able to say, that his views are those of the profession generally in this region, so far as I have been able to learn their opinions.

The weight of such widespread opinions directed against the use of ether because of the novelty of its activity or because of the suggestion of commercialism had its effect, and the use of ether was greatly curtailed in this country. This was recognized as early as 1848 in the report[10] of the committee on surgery of the American Medical Association, which stated concerning anesthetic agents:

This indifference to the discovery [in America] was probably owing to several causes. One of the most prominent of which was the taint of charlatanism which attached itself to its early history, and which caused a prejudice against it, in some minds so strong as to prevent them from giving the subject a full investigation. . . . The fault lies more with the discoverers, who attempted to conceal the nature of this new agent under the name of "compound letheon," than with the profession. Another reason why etherization was slowly adopted, was the instinctive fear of any agent which produced such peculiar and apparently alarming effects.

But as time passed, and as enthusiastic reports of the use of ether returned from England and the Continent, the popularity of ether seemed destined to increase, and its opponents found themselves in the unpleasant position of being forced grudgingly to use the product.[2] At this juncture the discovery of the anesthetic effects of chloroform was announced.

THE EARLY REACTION TO CHLOROFORM

Bigelow[1] came close to the discovery of chloroform; he had tried chloric ether with some success, and had he pursued the matter further would have realized that this article was nothing but a mixture of chloroform and alcohol. J. C. Warren[11] had also used chloric ether in the early days of etherization, but without complete success. It remained then for Simpson[12] to try the effects of undiluted chloroform, and to report enthusiastically that (1) it was more concentrated than ether, (2) its action was more rapid, (3) it was more agreeable to take, (4) it was less expensive because more concentrated, (5) there was no unpleasant odor clinging to the garments of the physician

after its use, (6) it was more portable, and (7) no special apparatus was required for its administration.

The first public notice of the new agent to appear in Boston was in the last number of the *Boston Medical and Surgical Journal* for 1848, in the form of a letter from C. A. Harris,[13] of Baltimore, as follows:

> Prof. Simpson of Edinburgh has lately published a pamphlet upon the use of chloroform as a substitute for ether in preventing surgical pain. A friend sent me a copy of it the day it was published, and I have experimented with the article before the students of the Baltimore Dental College. Although the tests have not been complete, as indeed they could not be in the few trials of a new agent in the use of which it was necessary to acquire dexterity and exercise prudence, I am satisfied that chloroform is much superior to ether and not liable to similar objections. I send, with this, a proof sheet of the *American Journal of Dental Science,* containing Dr. Simpson's account of this new agent.

At the same time Buckminster Brown[14] reported Simpson's discovery, although he had not yet submitted it to a trial. It was in fact Morton[15] himself, using a supply rapidly compounded for him by E. R. Smillie, who first employed chloroform in Boston. Under the influence of the material "teeth were extracted without the knowledge of the patient, and we would say that the effects were similar to those produced by ether." H. I. B.,[16] recognizing that chloroform was "pure chloric ether," wrote that its properties were identical with those of sulfuric ether.

The success of chloroform was immediate. The novelty of anesthesia had worn off, and there was little opposition on this score in America. It was introduced in a thoroughly reputable manner by a physician of great reputation, and with it anesthesia was easier to induce than with ether. In the rush to chloroform the lead was taken by the enemies of ether,[17] who thus were able to use anesthetics without being compelled to recant their vituperations against ether. A final letter from Flagg[18] illustrates this perfectly:

> The chloroform is an article which I have looked for in the last twelve months, with what I might call prophetic hope, and which I am now glad to possess as a substitute for the ether. I have used it in my operations ever since it was to be obtained here, almost every day, and some days three or four times; and always with as full an effect to dissipate the sense of pain as I have ever seen from ether, and without any, even the *slightest,* unpleasant symptoms.

This whole-hearted endorsement of chloroform was dated January 21, 1848, and thus Flagg could have had but three weeks' experience with the new agent!

If the enemies of ether became chloroformists, the etherists themselves were no less ready to give it a trial. As has been seen, Morton was the first to use it in Boston, and soon Bigelow[19] wrote again concerning its use:

> I have had a good opportunity of testing the effects of chloroform in my own and other operations, *and have used no ether since its introduction.* It seems to be thus far identical with ether in its effects: much stronger and portable (I should say two ounces would go as far as a pint of ether, that amount of each being sold at 75 cents). It does not infect the clothes, is less irritating to the lungs, and is at first quite palatable to the patient. It must, I think, supersede "ether," of which it is but a variety.

This is exactly what did happen, not only in Boston but elsewhere in America. Advertisements[20] for chloroform inhalers rapidly appeared until the editor[21] of the *Boston Medical and Surgical Journal* protested that . . . "like Connecticut washing machines the patterns of these instruments have become too numerous."

Then appeared the statements:[22]

> Messrs. W. B. Little & Company, Hanover Street, Boston, are manufacturing this new agent in large quantities. Much of it is packed up in phials small enough to be carried in a vest pocket, and secured at the cork in a manner to prevent loss by evaporation. . . .
>
> Dr. C. T. Jackson, the chemist, whose reputation is as extensive as the boundaries of science, speaks with entire confidence of the purity and excellence of Mr. Little's chloroform for all the purposes for which it may be required.
>
> The demand for chloroform almost exceeds belief—and we are almost disposed to ask under what circumstances it can be used.

Messrs. Little and Company reprinted a report by Simpson,[23] and appended a letter from J. Mason Warren advocating the use of chloroform. At the Massachusetts General Hospital,[24] where ether had been used in 132 cases to January 1, 1848, and from then to May 12, 1851, in 186 cases, chloroform and chloric ether were employed in 163 cases. Between January 1, 1848, and March 31, 1848, chloroform was used thirteen times and ether only eight times.[25] At Bellevue Hospital in New York, chloroform alone was used in the Second Division after January 3, 1848, until the time of a report[26] on March 3, 1848. The editor[27] of the *Boston Medical and Surgical Journal* commented upon this report that "it is gratifying to find the evidence in its favor increasing, especially when that evidence is furnished by the use of the article in skilful and judicious hands." The professor of surgery at Cincinnati[28, 29] reported his complete satisfaction with chloroform. Ether was almost "buried in oblivion."[30]

It is thus obvious that chloroform received a warm welcome at the hands of Boston physicians, not alone from the numerous opponents of ether, but from the very surgeons and dentists who had been responsible for the introduction of ether. No

trace of local partisanship for "Boston notions" was to be detected. On the contrary,[31]

> The beauty of the article [chloroform] and the rapidity of its influence gave it an immediate and general currency; for not only was it employed by physicians, but the community took the narcotizing drug into their own hands, and from the highest to the lowest indulged themselves in the chloroform excitement.

SUDDEN DEATH FROM CHLOROFORM

"We were soon awakened," continued J. C. Warren,[31] "from our dreams of the delightful influence of the new agent, by the occurrence of unfortunate and painful consequences, which had not followed in this country on the practice of etherization."

The issue of March 29, 1848, of the *Boston Medical and Surgical Journal* carried a report[32] of an unusual occurrence, first published shortly before in the *Lancet*.[33] A young girl in Newcastle, Hannah Greener, had visited a surgeon to have a toenail removed because of an onychia. A very small amount of chloroform (no more than a teaspoonful) was administered, and before she was completely unconscious the surgeon proceeded to the incision. She struggled as the operation began and then suddenly collapsed. Restorative measures were undertaken immediately, but in vain; in an entirely unexpected fashion she had suffered immediate death.

While discussion raged about the cause of death, and while Simpson[34] argued that it was probably due to asphyxia by drowning from the brandy poured into the victim's throat in an attempt to revive her, a second death[35] occurred under almost identical circumstances—this time in Cincinnati on the service of Dr. Mussey, an early adherent of chloroform.

The impression created by these two sudden deaths from chloroform was so great, that when a third occurred in Boulogne, the Minister of Public Instruction[36] invited the French Academy of Medicine to investigate the subject. A report presented by Malgaigne, the president, entirely absolved chloroform from any responsibility for the fatal accident on the grounds that the small amount of chloroform taken (5 grams!) and the extreme rapidity of death could not implicate chloroform, which could endanger life by asphyxia alone. To the publications of this report Guérin took violent exception, and insisted that in some fashion as yet unknown, chloroform was directly responsible for the deaths. Dispute between Malgaigne and Guérin became so acrimonious that a challenge to a duel[37] was passed, but was not accepted.

Reviewing the deaths to date, the *Medical Gazette* stated:[38]

> There was no asphyxia here; it could not be supposed that the deceased died from the effects of treatment. . . . . The most startling features of this case are that a person may very suddenly die from the effects of the vapour, without the occurrence of any one warning symptom to indicate the near approach of death; and that the vapour will prove fatal in cases which appear perfectly favorable to its administration.

While journals[39, 40, 41, 42, 43] continued to report more fatal and near-fatal cases of collapse under chloroform the *Boston Medical and Surgical Journal* made a restrained statement[44] tending to maintain confidence in chloroform as follows:

> The foreign medical journals contain accounts of deaths which have taken place after the use of chloroform — some of which were apparently caused by the use of that article in unsuitable cases and others in all probability had no other connection with such use than that of merely succeeding it.

Deaths from chloroform continued to be reported[45, 46] from all countries, and finally one occurred in Boston, not during surgical anesthesia but during self-administration to produce intoxication.[47] In this case, as in the majority of others, the amount of chloroform required to produce the fatal result was surprisingly small (3 drachms).

The Boston anesthetists were by now fully convinced that a peculiar unforeseen and unavoidable cause of fatality resided in the use of chloroform as an anesthetic. Their ample experience with ether proved to them that it was possible to produce complete surgical anesthesia with ether without any such fatalities, and that although death could result from asphyxia due to overdosage of both chloroform and ether, the sudden deaths reported occurred only after use of chloroform. In this, the lead was again taken by H. J. Bigelow,[48] and Warren[49] wrote with the greatest fairness:

> I hope it will not be thought presumptuous in me to propose the substitution of ether for an article which, although so deleterious to some individuals, has been, and still is, extensively used with safety on others. My apology must be found in the reflection, that, for more than a year before the introduction of chloroform, the ether-practice was carried on without any fatal results; that several fatal cases from chloroform occurred in a much shorter space of time than that above mentioned; and that a number of practitioners will feel absolutely compelled to abandon the use of these anesthetic agents, if chloroform be looked to as the principal.

In another place he[50] urged:

> In the mean time ether is used freely, daily, and harmlessly. No ill consequence worthy of record has fallen within our knowledge; but on the contrary its usefulness becomes more obvious in proportion to our experience of it. . . .

Soon afterward, George Hayward,[51, 52] who on November 7, 1846, performed the second operation under ether in Boston, wrote that chloroform, with twenty deaths to its credit already, must be considered a dangerous agent, and cautioned that chloric ether must also prove to have similar lethal

properties. Morton[53] also called attention to the dubious safety of chloroform and to the unquestioned safety of ether. Since their anesthetic properties were identical, he recommended the abandonment of the use of chloroform, and the exclusive use of ether. "No one," he said, "is justified in submitting his patient to the risk of his life by chloroform, simply because it is more agreeable, more powerful, cheaper, and more portable."

This position he[54] again stated in the *Boston Medical and Surgical Journal*:

> There is no reason for diminution of confidence in the *efficiency* and perfect *safety* of sulphuric ether; while there is an unanswerable reason why *chloroform* should be abandoned, as it involves the risk of a *fatal result*, which can neither be foreseen nor *prevented*. . . .

These clear warnings were in no way sufficient to stem the use of chloroform, and with grim regularity the *Boston Medical and Surgical Journal*[55, 56, 57] continued to describe in an almost stereotyped manner each new death: the great care of the chloroformist to avoid overdosage, the excitement or struggle, the reapplication of the chloroform, and the collapse and sudden death. In 1852 the same formula was used to describe[58] the death of a sailor in the Marine Hospital at Chelsea, where the anesthesia was so light that the victim reached for the chloroform sponge, took a single breath and fell dead. Shortly afterward, a death[59, 60] occurred in New Haven, and one[61, 62] in Boston. The latter was caused by chloric ether, and was followed immediately by another[63] in Boston, one[64] in Stamford, and one[65, 66] in East Lyme. Finally a death[67] took place on J. C. Warren's service at the Massachusetts General Hospital, where a bottle of chloric ether was by error filled with pure chloroform.

When several months later still another fatality took place in Boston, a coroner's jury recommended[68] that the use of chloroform be abandoned.

BOSTON VERSUS CHLOROFORM

At this juncture the Boston Society for Medical Improvement named a committee to study the properties of ether and chloroform, and especially to determine whether objections could be raised against ether similar to those directed against chloroform. This committee was able to collect forty-one cases of death alleged to have been caused by ether,[69] of which only nine took place during the operation itself. Seven of the latter were sudden deaths, and in all seven chloroform was combined with ether in the anesthetic mixture, administered subsequent to the ether or the "ether" employed was, in fact, chloric ether, a mixture of chloroform and alcohol. The report[70] concluded (1) that ether employed to produce anesthesia in surgery was less dangerous than chloroform, (2) that anesthesia was obtained as constantly and as completely by ether as by chloroform, and (3) that if ether presented the inconveniences which chloroform offered to a less degree, these inconveniences were of slight importance, and did not compensate for the danger inherent in the employment of the latter.

Encouragement in this position came shortly afterward in the statement[71] from Lyons of the superior safety of ether, and the abandonment of chloroform. In Lyons the experience of Pétrequin had been similar to that of the Boston surgeons. He had been one of the first to employ ether, and when chloroform was introduced, rapidly recognized its dangers and returned to ether. Before long he reconverted to ether all his great Lyonese surgical colleagues. With Diday, Gensoul, Bonnet and Barrier he made Lyons a center of etherization as well known in Europe as Boston was in America and England. While deaths from chloroform multiplied in every other hospital on the Continent, Pétrequin was able to report[72] that in fifteen years no patient at the Hotel Dieu at Lyons had died from ether. By his repeated statements[73, 74] of the reason for the Lyonese preference for ether, he played an important part in the reintroduction of ether into France and Italy.[75] On the whole, however, not even American opinion wavered greatly from its adherence to chloroform,[76] and the Civil War soon diverted attention to other matters.

In 1869, however, the editor[77] of the *Boston Medical and Surgical Journal* reopened the subject by a short statement of the reasons for the local preference for ether, and distrust of chloroform. This was followed by a short and unpleasant exchange of letters[78, 79, 80, 81] between Jacob Bigelow and Sir James Simpson, in which Sir James, only a few weeks before his death, gave ample credit to the Boston anesthetists but avoided the matter of sudden death in chloroform anesthesia.

Finally the *British Medical Journal*, which in England had been aroused by repeated chloroform deaths, precipitated an active controversy, although no mention of ether as a possible substitute for chloroform was made, by concluding:[82]

> So far as we have yet gone, it seems very probable that chloroform will hold its place with the British profession as being the safest anesthetic, which combines the recommendations of durable effect, rapidity of influence, suitability to all ages and states of health, freedom from after-consequences, and ease of administration.

This provoked a vigorous outburst[83] from Boston headed "Homicide by Chloroform," which concluded:

> Why not call the administration of chloroform for such purposes by its true name, homicide, since there is an agent, equally effective, and known to be perfectly

safe. Yet one would think, on reading British medical periodicals, that such a thing as a sulphuric ether was entirely unknown in the United Kingdom. A trial for manslaughter with a New England jury would bring British practitioners to a quickened sense of responsibility in the matter, and prove an effectual remedy to the recurrence of any similar "unfortunate circumstances."

To this the *British Medical Journal* replied[84] tolerantly that "the article from which we have quoted reads too much like the production of a partisan," and so dismissed the discussion of the possibility of a substitute for chloroform. For their indifference to ether, in the face of the known dangers of chloroform, British practitioners were taken to task by the *Boston Medical and Surgical Journal*.[85] Finally the editor,[86] with a great sense of the dramatic, inserted a notice that "after this week we shall not publish the details of these frequently occurring cases which may appear in other journals, but merely give the name and date of the journal in which they may be found."

The continuance of chloroform deaths in England, despite the greatest efforts to prevent them, led the *British Medical Journal*[87] again to plead for more complete records in chloroform deaths, and at last to suggest the substitution of other anesthetic agents for chloroform:

> The exclusive use of chloroform is almost confined to this country. We are disposed very earnestly to plead for a more extended employment of ether and of protoxide of nitrogen. Nothing has yet been found to rival chloroform for universal convenience; but convenience may be too easily purchased. It is, if the price paid seems to involve a sacrifice of life — and of life doubly sacred to us because specially entrusted to our keeping. On these grounds, we urge a revision of our customary anesthetics in this country; and, as the facts lie before us, they support the absolute interdiction of chloroform for dental extractions, the substitution of protoxide of nitrogen for these and for minor surgical proceedings such as we have indicated, and the substitution of ether for chloroform inhalation over a large range of surgical cases. What we may lose in convenience we shall gain in safety.

This frank change of opinion did not satisfy the *Boston Medical and Surgical Journal's* editor, and "Innominatus"[88] insisted:

> Why stop, in practice, to inquire why and how chloroform kills? It kills! and kills often, mixed or unmixed, pure or impure, with and without alcohol, and when given by the most experienced to the healthiest and heart-whole subjects. Is not this enough?
>
> Ether never kills in such circumstances — nor unquestionably in any other so far as known.

A succinct note[89] in the same issue stated: "In continuance of our plan to note the occurrence of deaths from chloroform, we give below a list of those observed since our last publication, June 15th." In that week ten new deaths had been reported.

The reason for the reluctance of British practitioners to employ ether and their persistence in using chloroform seems to have been twofold. In the first place, their experience with ether was limited, and they had no real reason to believe that it was any safer than chloroform except the word of the members of the Boston group whom they suspected of prejudice. In addition, their fear of chloroform had led them to be sparing in their use of it and to maintain a very light anesthesia. These precautions applied to the use of ether led to an unsatisfactory anesthesia, and prevented them from giving ether a fair trial.[90] The *British Medical Journal*, aware of this, started a campaign[91] to reopen the subject and to reintroduce ether to England. Soon afterward, it again strongly urged[92] the use of ether in place of chloroform:

> In face of the great mortality from chloroform and the almost deathless record of ether, it has become our duty to interpose, to call the urgent attention of the professional men throughout the country to the claims which ether has upon their confidence, and to urge that the anesthetic which was thrust out of repute by the ready and convenient fluid introduced by Simpson, shall have an extended and fair trial.

These extremely satisfactory evidences of a turning tide toward ether the *Boston Medical and Surgical Journal* warmly applauded, and added[93] that "if the British Medical Profession do not give ether a fair trial, after all that has now been told them, they will deserve the reprobation of the civilized world."

A rapid return to ether could not be expected. The deeply ingrained preference for chloroform was manifest even in Boston, where in the next few months two deaths from chloroform took place.[94,95] The indifference of the general public is shown by the fact that the *Boston Advertiser* reported[96] the first as a "death from ether," and only later corrected the error.[97] Surgeons did, however, begin to study the matter, and not a few visited the Massachusetts General Hospital to witness at first hand the Boston practice of etherization. Most of them were surprised at the freedom with which ether was administered.[98] The *British Medical Journal*[99] quoted them as saying:

> In Boston, ether was extensively used. At the Massachusetts General Hospital, ether was given with most absolute freedom, confidence, and apparent recklessness: in fact, when patients were brought into the hospital after accidents, the porter was in the habit of etherizing them even before they were seen by the house surgeon.

It seems almost certain that the freedom from accidents associated with the use of ether as opposed to the greater risks of chloroform was the essential factor in the evolution of the trained nurse as the anesthetist in America, and the qualified medical practitioner as the anesthetist in England.[100]

The persistent efforts[101] of the *British Medical Journal* in favor of ether then became as warm as

any Boston editorial, and soon produced both favorable and unfavorable reactions.[102, 103] A certain Dr. Skinner,[103] commenting on the visit to England of Dr. Fifield, of Boston, wrote:

> Ether is an American discovery; hence the national memorial being raised to Wells, the discoverer of its anesthetic properties, and deservedly. Now, Sir, would you be surprised if I told you that Dr. Fifield is surcharged with this same purblind American prejudice against chloroform in spite of what he says?

He quoted a Boston friend as stating that it would be as much as a man's life or his reputation was worth to administer chloroform in Boston, or almost anywhere in the United States. Although the deaths from chloroform in Boston clearly showed that there was much less local prejudice than he supposed, and although his quotation was denied by his Boston friend[104] and by Dr. Fifield,[105] Dr. Skinner[106] had the last word: "It must not be forgotten that there is such a thing as 'buncum' in America, and that it is cheap, and sold wholesale."

To these and similar evidences of a persistent prejudice in favor of chloroform, and ignorance of the administration of ether, the *Boston Medical and Surgical Journal* continued to reply editorially,[107, 108, 109] though with decreasing frequency, as the need grew less. A new generation of Boston practitioners grew up who knew little of the true facts, and used ether only because they had never been taught any other anesthesia. To them the attitude seemed ridiculous, and they started in again to use chloroform.[110, 111] The *Journal* occasionally wondered why the foreign countries insisted on using chloroform to some degree,[112] and largely forgot its historic opposition to chloroform in an eulogy of Simpson on the occasion of the centenary of his birth.[118] The controversy had come to an end in the practical victory of ether, and Boston could afford to be generous to an agent which retained but a fraction of its former adherents, and fortunately claimed because of this, and this alone, only a fraction of its former victims.[114]

The Mechanism of Sudden Death from Chloroform

Chloroform the Cause of Death

The astonishing rapidity with which death occurred under chloroform, and the almost unbelievably small amounts of the drug administered in fatal cases, led many anesthetists to deny that chloroform was in any way connected with the death. This was true of Simpson,[34] who analyzed the report of the first victim, Hannah Greener, and suggested that syncope having occurred because of the operation, or because of the chloroform, or both, the patient was asphyxiated by the well-intentioned efforts made to revive her—pouring brandy down her throat, and so forth. A French committee headed by Malgaigne arrived at a similar conclusion, and attributed the sudden death to some extraneous factor.[36]

The possible causes of sudden death suggested were in most cases fright,[115] or shock from the operation. Simpson[116] himself made use of such arguments when, in 1870, he was forced to report the death of a patient to whom he had himself administered chloroform. It is true that sudden, inexplicable death was recognized at that time, and may have been the cause of a few of the deaths, yet as case upon case came to be reported, in all of which chloroform had been used as the anesthetic agent, it became increasingly difficult to maintain that chloroform was completely innocuous. It is seen that Simpson himself believed this for more than twenty years, and there is no evidence that he ever admitted any danger from chloroform other than overdosage. Such an attitude is explicable only because such deaths were relatively rare, and because an individual anesthetist rarely saw more than a single death, and most physicians never saw any, even in a long practice. Unless they followed the literature carefully, it would be difficult for them actually to believe that chloroform could kill suddenly, and without warning. This is illustrated by an article by Keefe,[117] of Springfield, Massachusetts, in the *Boston Medical and Surgical Journal* as late as 1895.

> The idea that six minims of chloroform would kill a healthy man forty-two years old, or that a few drops would cause the death of a woman twenty-five years old, even though all air were excluded, is preposterous, and I for one will not believe it. Neither will I believe that two drachms, or eight grammes, if properly administered, will kill a *healthy* man. Fear alone, or acting in conjunction with the excitement and a disease necessarily fatal in itself, is what dealt the fatal blow. Thus is shown the fallacy, unreliability, and general unworthiness of the statistics relating to anaesthetics.

Other anesthetists attributed the fatal accidents with chloroform to the presence of impurities. This is the implication of Sédillot's[118] famous aphorism "Le chloroforme pur et bien employé ne tue jamais." Jackson[119] thought at one time that the contamination of chloroform with fusel oil was the lethal factor. Numerous careful chemical studies of chloroform employed in fatal cases failed to uncover any impurity that could possibly cause sudden death.[74, 120]

Keefe's[121] suggestion of disease necessarily fatal in itself was also seized upon very early as an explanation; autopsy reports began to a surprising degree to mention the "flabby myocardium" or the "fatty heart" found upon postmortem examination of the victim, until such reports were frowned upon and ceased to appear. Finally Sansom[122] made a careful study of the type of patient who died under anesthesia, and found that if anything

it was the vigorous, healthy individual who was more likely to succumb to chloroform than the ill or enfeebled one. Furthermore, the steady accumulation of an ever-increasing number of deaths under chloroform made the conclusion inescapable that this agent was itself the direct cause of death. The mechanism of such death, however, remained unknown.

DEATH FROM OVERDOSAGE

Most anesthetists, even in the ether period, quickly learned that if the agent were given to excess, respiration would stop, and death might ensue from asphyxia. In practically all cases, however, it was possible to obtain complete and rapid recovery simply by ceasing administration of the drug and applying restorative measures. Animal experimentation showed that even after cessation of respiration the heart continued to beat, and as long as the pulse remained, resuscitation was possible. Recognizing this, a great number of anesthetists attributed chloroform deaths to asphyxia from overdosage. This is the implication of reports by Malgaigne,[123] Cummings[124] and Cartwright,[125] and constituted one of Claude Bernard's most serious errors.[126]

The immediate result of these opinions was a great number of careful studies of the effect of various percentages of chloroform vapor. The first of these was by a committee appointed by the Royal Medical and Chirurgical Society to study the "physiological, therapeutical and toxical effects of chloroform." This committee, which included James Paget, George Harley, Richard Quain and others, reported[127, 128] that the cause of fatality resided in an excessive concentration of chloroform, and that for comparative safety the vapor should not be more concentrated than 3.5 per cent. They obviously used the dilution technic in a study of ether, because they reported that it was slow and uncertain in its action, and although they conceded its superior safety, they concurred "in the general opinion which in this country has led to the disuse of ether as an inconvenient anesthetic." A note of dissension was struck in the discussion by Dr. Kidd,[128] who called attention to the fact that human beings did not die in chloroform anesthesia from the deep asphyxia that killed the experimental animals, and stated that from the report of the committee it seemed paradoxical that chloroform administered in small doses should be dangerous.

Despite the clear evidence that chloroform death was not due to asphyxia, the idea persisted, possibly because it was the one tangible finding produced by any study. As a result, anesthetists became increasingly careful in their administration, and a great variety of systems were devised to reduce the concentration of chloroform vapor to a minimum. Despite these precautions, deaths continued, and another complete study was made. This was financed by the Nizam of Hyderabad, whose physician, Edward Lawrie,[129] had reopened the matter by investigations which seemed to prove that asphyxia alone was the cause of chloroform deaths. These findings being challenged, the Nizam defrayed the costs of a second commission, composed of Lawrie, Lauder Brunton, who was appointed by the British Medical Society, and two others. The committee traveled to Hyderabad, and after a new series of experiments again reported[130] that asphyxia alone caused death. Regarding "sudden death," they[131] said:

> The deaths were not really sudden, but only rapid, and the result of reckless administration of concentrated vapor in the first instance, and careless neglect of the respiration in the second. There is no evidence whatever that one single one of them was due to paralysis or sudden stoppage of the heart, as Snow assumes to be the cause.
>
> The Hyderabad commission has proved that there is no such thing as chloroform syncope, and that in death from an overdose of chloroform the respiration always fails before the circulation. . . . In the telling words of Dr. Bomford it is sufficient for us as practical men to know (1) that the heart is the very last organ to give in under the action of chloroform, and (2) that there is no more danger of permanently paralysing it in chloroform administration, than there is of paralysing the legs and giving the patient a diplegia.

These opinions were corroborated in their essentials by Gaskell and Shore,[132] who also performed animal experiments, and concluded that the danger in chloroform anesthesia was from overdosage, and that overdosage caused both respiratory paralysis and cardiac weakening. With their last statement Brunton[133] disagreed, and claimed that "they [Gaskell and Shore] entirely confirm the conclusions of the Hyderabad Commission that the chief danger from chloroform is the concurrence of asphyxia, and that the most important practical point is the attention to respiration, as maintained by Syme and Lister."

The Nizam of Hyderabad financed another investigation, by Hare and Thornton,[134, 135] who, although they disagreed with minor portions of the Hyderabad report, concluded by stating positively that chloroform kills by respiratory failure.

Still another "chloroform committee," of which Sherrington and Sowton were the physiologists, again insisted that the essential danger in chloroform anesthesia was overdosage, and recommended still lower concentrations. Even 2 per cent of chloroform in the vapor was said to be dangerous.[136, 137] Waller[138] reiterated that all deaths from chloroform were due to excessive chloroform, and also suggested 2 per cent chloroform vapor as the maximum safe dose.

As late as 1908, the Commission on Anesthesia[139]

of the American Medical Association still clung to the notion of overdosage: "We therefore conclude that all of the accidents of chloroform are due to overdosage. That this is so is shown by laboratory experiments." This committee was little bothered by the clear evidence that this could not possibly have been the case, but at least made an attempt to reconcile facts with their theory. Their explanation of the sudden death in chloroform anesthesia was that the patient made a sudden deep inspiration, thus taking into the lungs a high concentration of vapor, which was sufficient to cause overdosage and death! Neither they nor the members of any other committee undertook to explain why "overdosage" of ether never took place under similar circumstances, nor why it was almost never possible to revive the patient from this so-called chloroform "overdose" as it was after an overdose of ether or, in fact, after a true overdose of chloroform in experimental animals.

However strongly such theories were put forward, their falsity was inexorably and incontrovertibly demonstrated. Anesthetists strove with renewed zeal to administer the smallest possible concentrations of vapor at all consistent with anesthesia; but the results so far as chloroform fatalities were concerned remained the same as reported in 1859 by George Hayward,[140] who, after a graphic description of the second operation in Boston under ether, which he performed, wrote:

> The truth is, that chloroform, when inhaled, acts on the system in a way that is not well understood, and may destroy life in spite of the utmost caution. Its effects are sometimes so sudden, that no foresight can prevent a fatal result.

Statistics presented by Silk[141] in 1892 showed that from twenty to thirty-six deaths from chloroform occurred annually in England alone between 1880 and 1890. Deaths in Scotland and Ireland were not included.

THE MECHANISM OF DEATH

Deaths with Low Concentration. The one outstanding fact in the case reports of chloroform deaths was the minute quantity of chloroform inhaled, and the extreme lightness of the anesthesia produced. It was reported[142] that the last words of Mrs. Crie, a Boston victim of chloroform, were: "The only fault I find with Dr. Eastman is that he never gives me enough." The story of the sailor at the Marine Hospital in Chelsea who was conscious enough to reach for the sponge and take the fatal breath himself is also typical. It is almost unbelievable that the theory of overdosage could have developed at all, much less persist as it did for over fifty years.

The Boston anesthetists were never in doubt as to the clear distinction between death from asphyxia and sudden death from chloroform. Their considerable experience with ether, and the liberality with which they applied it, must have provided them with a very ample acquaintance with asphyxial symptoms in their patients. As early as 1848 Bigelow[143] clearly distinguished between the symptoms of asphyxia and those of chloroform syncope, in which, he said, chloroform seemed to produce "a sudden and overwhelming shock upon the system." Warren[49] wrote a year later:

> In a large part of the fatal cases, one fact at least is conspicuous; and that is the suddenness with which the fatal phenomenon occurred. . . . When we compare these sudden effects of chloroform with those from its continued use in cases of prolonged operations, it seems quite clear that the fatal issue is not a consequence of the quantity inhaled, nor yet of the time, but rather of the instantaneous violence of its application.

Morton[53] wrote in 1850 that "there are certain idiosyncrasies, which cannot be known in advance, in which a very minute quantity of chloroform has produced, and will again produce, death."

Other anesthetists[144, 145] recognized the same facts. In England, John Snow, who had written[146] on ether anesthesia in 1847, carefully distinguished between asphyxial and sudden chloroform deaths in his monograph[147] on anesthesia published in 1858. He also insisted that in chloroform death sudden failure of the heart was the essential cause of collapse, and that respiration stopped only after cardiac arrest, while in asphyxia cardiac activity continued long after respiratory paralysis. These two facts, that death is produced with low concentration of the vapor and light anesthesia, and that death is due to sudden failure of the heart, formed the basis for the correct solution of the problem of chloroform syncope. Although they were both clearly enunciated before 1860, it was fifty years before the final solution was worked out.

Cardiac Paralysis. It was naturally supposed that the sudden failure of the heart was caused by its arrest;[148] Snow[149] and others spoke of it as a sudden paralysis of the myocardium. The mechanism of such arrest was, however, not clearly formulated, and both a direct action of chloroform on the heart and an indirect action on the cardiac nerves were suggested. The discovery of the inhibitory effect of the vagus nerves, when directly or reflexly stimulated,[150, 151] was utilized by many to explain the sudden cessation of cardiac activity[152, 153, 154], and though evidence appeared to indicate some degree of vagal activity in chloroform narcosis,[155, 156, 157] the hypothesis found little support, especially since inhalation of ether, alcohol, fumes of ammonia and so forth produced similar vagal effects[158, 159, 160]. This theory was,

however, directly responsible for the introduction of atropine as a preliminary medication in anesthesia. By its use it was hoped to suppress the sudden excessive vagal stimulation and syncope; and while it failed to prevent chloroform deaths, its value in prevention of mucus formation was quickly recognized.[161]

An interesting development of the theory of cardiac arrest was the use of galvanism to revive the supposedly arrested heart as well as to stimulate respiration.[162] In Boston, a dentist[163] used the galvanic battery to revive a patient who had collapsed under chloroform, and the committee of the Royal Medical and Chirurgical Society[127] listed galvanism as worthy of trial in syncope. It remained for Steiner[164] in Billroth's clinic to devise a method of "electropuncture" of the heart, in which a needle inserted into the heart became the positive pole in a stimulating circuit applying make-and-break shocks at intervals of a second. With this apparatus he claimed to be able to revive quiescent hearts of experimental animals, but a single attempt to resuscitate a young woman who collapsed under chloroform proved unsuccessful.

The theory of paralysis of the heart remained an expression of the clinical finding that the circulation failed before the respiration. It did not survive an accurate experimental analysis of the problem, which revealed the actual mechanism of the fatal collapse of the circulation.

Ventricular Fibrillation. In 1842, Erichsen[165] tested Marshall Hall's[166] suggestion that experimental occlusion of a coronary artery in a dog's heart might stop the action of the heart. Erichsen found that while such a procedure did in fact cause a rapid death, the heart did not simply stop beating, but instead the normal rhythm of the heart was replaced by a rapid inco-ordinate "tremulation" of the myocardium, which was incapable of maintaining a circulation. The same peculiar peristaltic cardiac activity was found in similar circumstances by Cohnheim and von Schulthess-Rechberg,[167] and by Hoffa and Ludwig[168] following faradization of the ventricles. It was also noted by Kronecker[169] following mechanical injury, and by many others.[170] The phenomenon was given such names as delirium cordis, arrhythmic fibrillar contractions, or as it is now called, ventricular fibrillation.

Recent summaries[171] of the course of this fatal arrhythmia demonstrate that it begins typically in a series of ventricular extrasystoles from multiple foci which progress to runs of paroxysmal ventricular tachycardia at increasing rates, and terminate in ventricular fibrillation and sudden death. During the early stage, therefore, the pulse becomes irregular, and with the onset of tachycardia and fibrillation the pulse is extinguished and collapse occurs. It is also found that this succession of events is not necessarily inevitable, and that even after fibrillation itself has started, a normal rhythm may return and a fatal outcome be avoided.

Few anesthetists in the early period watched the pulse of their patients, but it is remarkable that at least one physician[172] noticed cardiac irregularities in the early stages of aborted syncope during chloroform inhalation, and reported them in the *Boston Medical and Surgical Journal:*

> I have recently had two or three such cases. On inhaling a small quantity of a mixture of chloroform and ether, great irregularity of the heart became manifest, a disposition to syncope, a nameless dread, and so forth. In one case, the symptoms were present when the patient had not the slightest degree of fear about breathing an anesthetic.

MacWilliam[173] noted the onset of bursts of tachycardia during chloroform anesthesia in experimental animals, especially during induction and recovery, or at any time that the anesthesia became light, and especially if the animal struggled.

Schiff[174] in 1874 was the first to notice that after chloroform death in experimental animals the heart was not to be found in standstill, but that the entire heart was involved in many increasingly small fibrillary contractions, such as he[175] had also noticed after corrosive sublimate poisoning. The fibrillation in these observations was more than likely simply terminal fibrillation in an asphyxiated heart, as Ratimoff[176] pointed out in 1884. The same conclusion was drawn by MacWilliam[177, 178, 179] from his own observations on animals killed by overdosage. He said:

> The occurrence of fibrillar contraction (delirium cordis) does not appear to be a primary mode of cardiac failure from the inhalation of chloroform in the healthy animal, though it may sometimes supervene when the heart has become distended or incapacitated by chloroform.

The final resolution of the problem, harmonizing clinical and experimental findings,[180] was brought about by Levy. In a preliminary report before the Physiological Society he[181] outlined the three major phases of his solution of the problem. He found: (1) that in properly organized laboratory experiments, syncope and sudden death were produced during light chloroform anesthesia; (2) that the cause of the syncope was the sudden onset of ventricular fibrillation—a suggestion made by Cushny,[182] who had not been able to produce such sudden death in his own experiments; and (3) that intravenous injection of adrenalin was almost always fatal in light chloroform anesthesia, and that such death was produced by ventricular

fibrillation. In subsequent reports these three points were more completely elaborated, and their relation to the clinical problem was demonstrated.

In a very careful analysis of deaths from chloroform anesthesia in man, he[183] was able to show that in 87 per cent of the cases he studied there was definite evidence of the absence of overdosage, and moreover that in 47 per cent underdosage was certainly present.

With Lewis he[184] demonstrated the presence of ventricular fibrillation by means of the electrocardiograph. The electrocardiograms showed clearly the progression from isolated extrasystoles to ventricular fibrillation when small doses of adrenalin were administered during light chloroform anesthesia. His records were comparable to the first electrocardiograms of ventricular fibrillation taken by Kahn[185] and by Jolly and Ritchie.[186] Hill[187] and Busquet and Pachon[188] had suggested this earlier but showed no records.

Finally, he pointed out the important part played by adrenalin or sympathetic stimulation in the genesis of the fatal arrhythmia. He noted the extraordinary accident reported by Oliver and Schäfer[189] in their classic work on the extract of the suprarenal capsules. Oliver and Schäfer were testing the effect of their newly discovered hormone by injecting it into animals anesthetized by chloroform, morphine and atropine. They noted:

> In a single experiment, one of many which we have performed, the intravenous administration of the extract began by producing the ordinary effects upon the circulatory system. At the moment, however, when the blood-pressure had attained its full height the ventricle passed into a condition of fibrillar contraction from which it failed to recover.

Elliott[190] had noticed the same phenomenon in his later work on adrenalin. Next Levy called attention to an equally remarkable series of accidents[191, 192, 193] following the clinical use of adrenalin. Operations on the nasal septum had always been hampered by congestion of the mucosa, and it was soon found that adrenalin would blanch the region and permit more careful surgery. Naturally, the chloroform mask had to be removed during the operation, and thus anesthesia tended to be light. It was soon evident that this combination led to syncope, from which the patient sometimes recovered, yet might die. The amounts of adrenalin necessary to produce syncope were very small, no more than from 2 to 5 minims of a 1:1,000 solution.

Investigating this matter experimentally, Levy[194, 195, 196] found that a synergism existed between light chloroform anesthesia and adrenalin or the discharge of the sympathetic nerves to the heart. Chloroform or adrenalin alone produced only transient extrasystolic irregularities,[197] but when they were combined, ventricular fibrillation resulted. Direct stimulation of the accelerantes nerve, or stimulation of the splanchnic nerve, also produced ventricular fibrillation in the presence of light chloroform anesthesia. If the anesthesia was profound, fibrillation of the ventricles could not be produced, and asphyxia actually protected the animal against the combined effects of chloroform and adrenalin.

The effects of direct stimulation of the accelerator nerves of the heart and to the splanchnic fibers to the adrenal glands could further be produced reflexly with identical results. Thus it was finally demonstrated why excitement, struggle or pain so often precipitated syncope; because all these are procedures which reflexly stimulate the accelerator nerves to the heart and result in the liberation of adrenine into the blood stream. Factors restraining sympathetic activity, such as stimulation of the vagus nerve, protected the heart, while atropine, which paralyzes vagal influence, favored the appearance of ventricular fibrillation.[198]

The mechanism of chloroform syncope can be summarized[199] thus: (1) during the period of light anesthesia, the heart becomes hypersensitive to adrenine and the discharge of the sympathetic nerves in the heart; (2) the presence of excitement, struggle or pain during this period reflexly liberates adrenine and produces discharge of the cardioaccelerator fibers; (3) the combination of these factors produces fibrillation of the ventricles, which is the direct cause of death; (4) the sensitivity of the myocardium and the amount of sympathetic activity can at times be sufficient to cause syncope, even when struggle or excitement is not pronounced; (5) during full anesthesia, or in asphyxia, this mechanism is inoperative; (6) such a state never occurs with ether anesthesia.

Although with these investigations the problem of the mechanism of death was solved, the problem of chloroform remained. In each chloroform anesthesia, two periods of light anesthesia are necessarily found—during induction and during recovery. In these intervals the patient must be exposed to the dangers of syncope, and where chloroform is still used as an anesthetic, syncope is still reported.[108] While little can be done after fibrillation has once set in, reduction of the activity of the sympathetic nervous system by the barbiturates seems to be a rational means of prevention of syncope.[200]

Summary and Conclusions

1. The enthusiastic reception of chloroform by the opponents of ether was an important factor in the establishment of the early ascendancy of chloroform, but the greater convenience and ease of administration of chloroform quickly won over the strongest proponents of ether, and even in

Boston, chloroform was received without prejudice and was widely employed.

2. When sudden death was found to occur during chloroform anesthesia, Boston surgeons, because of their extensive experience with ether, recognized that this was an accident peculiar to chloroform, and began an active crusade to substitute ether for chloroform. Because of their activities, and because deaths continued to occur from chloroform despite the greatest precautions, the use of ether was renewed, and finally almost completely supplanted that of chloroform.

3. The mechanism of sudden death from chloroform was ultimately solved by Levy, who demonstrated that it was due to the development of ventricular fibrillation as a result of sympathetic discharge, or liberation of adrenine, during light chloroform narcosis.

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EFFECT OF AMNIOTIN AND ANTUITRIN-S IN DIABETES INSIPIDUS

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THERE has appeared experimental evidence suggesting that the administration of estrogenic substance may suppress the diabetogenic and sex principles of the anterior lobe of the pituitary gland.

The polyuric effect of certain extracts of the anterior lobe of the pituitary has been reported by a number of authors, among them Teel and Cushing[1] and Biasotti.[2] Consequently, it is believed that this gland secretes a diuretic substance. It seems of practical interest to determine whether the so-called diuretic principle of the anterior pituitary gland may be suppressed in a similar manner. Already there have appeared clinical investigations to substantiate this idea. Troisier[3] and Beltrametti[4] have injected large doses of folliculin into patients with diabetes insipidus and obtained a marked antidiuretic effect within several days. Omission of the folliculin resulted in a return of the polyuria. Astwood[5] also noted, following amniotin administration, a temporary improvement of the diabetes insipidus of a woman in whom menopause was induced artificially by irradiation of the ovaries five years previously. Duvoir, Pollet and Cachin[6] treated a patient with diabetes insipidus during the course of three pregnancies and observed in the sixth month of each that the polyuria decreased and the amount of urine became normal during the weeks preceding delivery. However, on the day following delivery the urine increased rapidly to 12 liters, the level before pregnancy. On the basis of the action of pregnancy on the polyuria they administered folliculin to this patient, which resulted in a reduction in the volume of urine again.

Allen and Stokes[7] reported a cure of diabetes insipidus coincident with bilateral correction of abdominal cryptorchidism in a boy following a series of twenty-five injections of 1 cc. doses of antuitrin-S during a two-month period. At the end of a month, however, after the fifteenth injection, the polyuria and polydipsia had disappeared.

This paper reports some observations in 7 patients with diabetes insipidus following the injection of large doses of amniotin* and of antuitrin-S.*

The plan of study consisted chiefly in observing the daily fluid intake and output before and after the administration of amniotin and antuitrin-S. In 5 cases 20,000 units of amniotin were injected daily for a period of ten consecutive days and incidentally the sugar tolerance was studied using a standard dose of 100 gm. of glucose. In

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*Amniotin is the estrogenic substance prepared from the urine of pregnant mares and amniotic fluid, by E. R. Squibb and Sons, who kindly supplied it for this investigation. Antuitrin-S is the standard gonadotropic factor or the anterior-pituitary-like sex hormone obtained from the urine of pregnancy.

4 cases 1 cc. of antuitrin-S was administered subcutaneously daily or every other day for a period of two months.

CLINICAL MATERIAL AND RESULTS

The persons studied were 3 men, 1 boy and 3 women who had had diabetes insipidus of idiopathic origin for a number of years. They were all relieved of the polyuria with the intramuscular or intranasal administration of posterior-pituitary-lobe extract (pituitrin). They were selected because they represented, except for the diabetes insipidus, a variety of individual types: 2 essentially normal young men, 2 males with marked sexual underdevelopment, a young woman before menopause, a woman beyond menopause and an obese woman after menopause without a thyroid gland.

Their cases are briefly presented as follows:

Case 1. A 22-year-old unmarried musician, who had had diabetes insipidus for 11 years. He was a very bright student at school and president of his class. His daily fluid intake and output usually varied from 12 to 14 l. a day. The physical examination was entirely normal. The basal metabolism was —9 per cent.

He was given amniotin with no change in the polyuria and polydipsia. However, he noted slight soreness of the breasts for several days at the end of treatment with amniotin. At this time the metabolism was —16 per cent. Two months later treatment with antuitrin-S was started. He was given 1 cc. every other day for 1 month and then daily for another month. This was followed by no changes in his symptoms of diabetes insipidus, although he gained several pounds in weight.

Case 2. A 25-year-old male laborer, who had had diabetes insipidus for 6 years. The daily fluid intake and output had been as high as 11 l. in the past. During the past 2 years, however, they had been at a fairly constant level of about 5 l. a day. The physical examination showed him to be about 15 lb. underweight. The skin was of the female type and there was only a slight amount of hair over the pubic region. There was considerable sexual underdevelopment, the penis and testes being small.

Amniotin was administered, with no decrease in the polyuria and polydipsia. His metabolism before and after amniotin therapy was —14 and —12 per cent, respectively. There was some soreness of the breasts for several days during the period of treatment. After an interval of 5 weeks, 1 cc. of antuitrin-S was administered daily for 1 month and then every other day for another month. The fluid intake and output remained much the same, except that 4 days after this treatment was instituted there was an increase of about 2 l. for a period of 10 days.

Case 3. A 23-year-old, unmarried schoolteacher, who had had diabetes insipidus for 5 years. Her daily fluid intake and output had been 12 to 14 l. a day. The menstrual history had been normal except that the intramuscular injection of pituitrin caused painful menses. The physical examination was negative except for being 15 lb. underweight. The basal metabolism was —19 per cent.

Amniotin therapy caused no change in her condition.

Case 4. A 56-year-old housewife, intelligent and somewhat nervous, who had had diabetes insipidus for 3 years. She had never had any children. She had gone through the menopause uneventfully 6 years previously. Her daily fluid intake and output usually varied from 8 to 10 l. a day. The physical examination was negative except for a blood pressure of 168 systolic, 100 diastolic, and slight prominence of the eyes.

She was given amniotin with no change in the fluid intake and output. Nevertheless, she became less nervous and her metabolism dropped from +12 to —14 per cent after treatment.

Case 5. A 68-year-old housewife, who had had diabetes insipidus for 6 years. She had eight children and had gone through the menopause about 20 years previously. The daily fluid intake and output had been 8 to 10 l. a day. She had had a total thyroidectomy on June 24, 1935. The details of this aspect of the case will be published elsewhere. The essentials of the physical examination were obesity, a moderately enlarged heart and some edema of the legs. Her height was 5 ft. and her weight 220 lb. The pulse was 72, and the basal metabolism —10 per cent.

The administration of amniotin produced no change in her condition.

Case 6. A 36-year-old male clerk, who had developed diabetes insipidus during the course of a severe septic sore throat 7 years previously. His daily fluid intake and output during the past 3 or 4 years had been about 7 l. The physical examination was normal.

He took 1 cc. of antuitrin-S every other day for 2 months with no essential change in the polyuria and the polydipsia. The patient noted, however, that there was an increase in saliva and that his mouth was not so dry. His weight increased 3 lb.

Case 7. A 14-year-old bright schoolboy, who had had diabetes insipidus for 9 years. His daily fluid intake and output had been about 7 to 8 l. for several years. He had a twin sister who was perfectly normal. The physical examination showed him to be considerably underdeveloped. His height was 57 in. and his weight 69 lb., compared with his twin sister's height of 64 in. and weight of 95 lb. The penis and testes were infantile, and there was no pubic hair. The basal metabolism was —9 per cent. X-ray examination of his head and right wrist indicated that his development was several years behind that of his twin sister.

He was given 1 cc. of antuitrin-S every other day for 2 months, with no improvement in the fluid intake and output or change in the size of the external genitalia. His weight increased 3 lb.

The fluid intakes and outputs in these cases remained much the same during the period of amniotin injection and also for a period as long as five months after the withdrawal of the drug. These observations do not confirm the findings of the investigators who obtained an antipolyuric effect in diabetes insipidus following the administration of estrogenic substance. It appeared, from these results at least, that amniotin did not depress the diuretic principle of the anterior lobe of the pituitary gland, nor did it act on polyuria in any other manner in the cases described. There were no remarkable changes in the general subjective feelings of the patients. However, 2 male patients noted slight soreness of the breasts for

several days at the end of treatment with amniotin, and in Case 4 the patient became less nervous.

Antuitrin-S also caused no improvement in the symptoms of diabetes insipidus as long as three months after the omission of the drug, although the patients gained several pounds in weight. It produced no change in the size of the external genitalia in the 2 males who had marked sexual underdevelopment.

Comparatively little is known of the effect of amniotin on sugar tolerance. However, certain observations have been reported to suggest that the drug has some influence on this phase of the metabolism. Barnes, Regan and Nelson[8] and Nelson and Overholser[9] have noted an improvement in experimental diabetes mellitus following the administration of amniotin. Collens and associates,[10] however, were unable to confirm this finding in clinical diabetes mellitus.

The sugar tolerance had been determined in the patients used in this study two to six times at varying intervals before amniotin was administered, and in each case the blood-sugar levels were much the same. The first sugar-tolerance tests reported in Table 1 were done shortly before starting amniotin. Since there was a decreased sugar tolerance in these patients, it appeared of interest to determine whether amniotin would alter the blood-sugar curves of such persons, and the test was repeated in 4 patients ten days after the amniotin had been begun. It was interesting to find that in each case there was a definite decrease in the blood-sugar curves after treatment with amniotin. No conclusions can be drawn, however, from tests obtained in only 4 cases; these curves are presented incidentally as a matter of interest.

TABLE 1. *Sugar Tolerance Tests in Patients with Diabetes Insipidus before and after Amniotin Administration.*

Case No.	Blood-Sugar Levels before Amniotin Therapy					Blood-Sugar Levels after 10 Days of Amniotin Injection				
	Fasting	*No. of Hours after Ingestion of Glucose*				*Fasting*	*No. of Hours after Ingestion of Glucose*			
		½	1	2	3		½	1	2	3
1	93	116	151	114	84	98	135	81	91	48
2	100	186	151	72	64	70	122	51	49	58
4	85	189	222	136	111	82	174	163	105	54
5	120	178	211	149	151	87	123	160	135	71

SUMMARY

This paper reports some observations on the fluid intake and output in 7 patients with diabetes insipidus following the injection of amniotin and of antuitrin-S. In 5 of these cases 20,000 units of amniotin was injected daily for a period of ten days. In 4 cases 1 cc. of antuitrin-S was injected daily or every other day for a period of two months.

The administration of amniotin or of antuitrin-S did not cause any decrease in the daily fluid intake and output of these patients.

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MALIGNANT TUMOR OF THE OVARY OCCURRING IN A THIRTEEN-YEAR-OLD GIRL

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NEOPLASTIC changes occur in the ovary less frequently than is generally supposed. The literature supports this statement and also brings out the fact that carcinoma of the ovary developing in the young female is a rarity.

Ewing[1] states: "Tumors of the ovary are not notably frequent. All ages are susceptible, from birth to senility, but the period of sexual activity, 25 to 35 years, is most prominent. Lippert refers to 58,787 female clinic patients of all types, among whom were 941 ovarian tumors, 1.6 per cent. Wiel collected 24 cases under 5 years, and 60 under 10 years of age, and Hubert 175 cases in children."

The Pondville Hospital (Massachusetts) treats malignant diseases only. A personal communication[2] summarizes the cases treated there. From 1927 through 1935 in approximately 7,000 admissions for malignant disease there were 79 primary malignant tumors of the ovary, making a percentage of .011 of the total. No case was under twenty years of age.

From another source[3] comes the following statement: "In a collection of 1,764 cases of tumors of the ovary, Olshausen found 61 cases below the age of 10 years. Hubert (1901) reported 175 cases of tumors of the ovary up to the age of 17 years. He found 115 benign, and 60 malignant tumors. Out of the malignant tumors, 28 were carcinoma (solid and cystic) and 32 sarcoma. Other statistics of 202 cystic tumors of the ovary in children showed 35 per cent cystoma, 31 per cent dermoids and 34 per cent malignant tumors. Sarcomas are more common in children than carcinomas."

Out of 12,260 admissions in ten years to the surgical service at the Children's Hospital, Boston, Lanman[4] reports 5 cases of ovarian tumor in children under twelve.

It is apparent that although malignant tumors of the ovary do occur in children, they are extremely rare.

The symptoms in the cases reported have been vague. In most instances, the true diagnosis was not considered, because the condition is infrequent, and therefore not usually anticipated. The final diagnosis in most instances was made by the pathologist, and in many of the reported cases even the diagnosis of malignancy was debated by the pathologists who examined the tissues. Lanman,[4] Ridout,[5] Rosenberg,[6] McNamara et al.,[7] Bland et al.,[8] Knewitz,[9] Best,[10] and particularly Burnam[11] emphasize these difficulties in diagnosis and classification.

The symptoms in the present case were in no way suggestive of a neoplasm of the ovary; much less were they those of malignant disease. Examination prior to operation did disclose an enlarged right ovary, but the most that could be said about it prior to operation was that it was abnormal in size.

CASE REPORT

The patient was a 13-year-old, white girl, one of three children. The family history was irrelevant.

Her catamenia had not been established, and there had never been any suggestion of menstrual flow. At intervals during the past 6 years she had been treated for infestation with *Taenia saginata*. An x-ray film of her lungs taken 1 month previously was reported negative. The patient had suffered occasional attacks of severe pain "deep inside and low in the abdomen," which were worse "when running."

About 9 p. m. on January 10, 1936, she was sitting in a chair with her legs hanging over its arm when she suddenly experienced a sharp pain, low down in the right side of the abdomen. The pain caused her to cry out, and disappeared in about 5 minutes. About an hour later she went to bed, but was awakened after about 2 hours of sleep by severe pain in the same region. Shortly afterward she vomited and was then seen by her physician, who found spasm and tenderness in the right lower abdomen, a normal temperature and a pulse rate of 90. In view of the findings, he suspected an attack of appendicitis, and advised immediate hospitalization. She was seen in consultation at the hospital at about 3 a. m.

Physical examination revealed a well-developed and nourished child, whose temperature was 98.6°F., pulse rate 90, and respirations 18. There was no discernible focus of infection in the nose, mouth or throat. There were no enlarged lymph nodes. The eyes were normal, as were the heart and lungs. Examination of the abdomen revealed tenderness in the right lower abdomen, halfway between McBurney's point and Poupart's ligament. There was a suggestion of slight spasm in this region. All other parts of the abdomen were negative to palpation. Examination of the external genitalia showed nothing remarkable. Rectoabdominal examination disclosed the cervix and uterus to be infantile in type. The left vault was negative; in the right vault could be palpated a very tender, freely movable, firm, hen's-egg-sized mass. The extremities, skin and breasts presented no abnormalities. The urine was normal.

In view of these findings, a diagnosis of right ovarian tumor was made, and because of the acuteness of the symptoms, it was decided to operate at once.

Operation was performed at 4 a. m. Upon incising the peritoneum, about 250 cc. of blood was immediately discharged from the abdominal cavity. Several large clots were also removed. The abdominal and pelvic cavities were sponged dry. No gross blood or bleeding was visible

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after this procedure. The right ovary was very firm, about three-quarters the size of a large hen's egg, and was ruptured for a distance of about two-thirds of its diameter. In the V-space of the rupture, blood clot had accumulated; in this region there was also present a yellow, rubber-like material. The remainder of the ovary

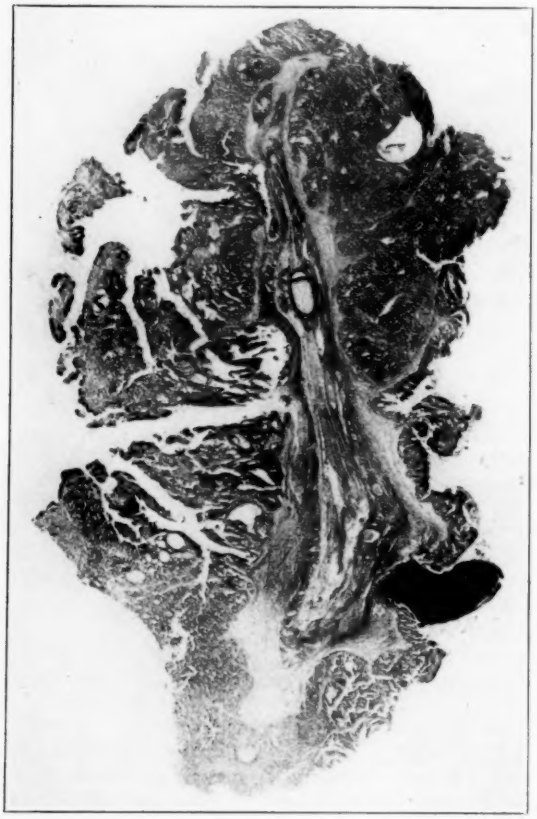

FIG. 1. Low power, showing a central streak of stroma and original ovarian tissue surrounded by the tumor, presenting a pseudopapillary arrangement. In the stroma near the upper end is a graafian follicle. At the lower right hand side is an area of hemorrhage and blood clot. 8×.

was firm, except in the region of some simple cysts. There were numerous pieces of this rubbery material in the pouch of Douglas. These varied in size up to that of a chestnut, and were removed. The ovary was removed. Examination of both fallopian tubes, uterus and left ovary disclosed no abnormalities. The peritoneum, bladder and all visible intestine appeared normal. The appendix buried in adhesions except for the tip, which was bulbous and appeared inflamed, was removed.

Pathological Report (Dr. M. J. Schlesinger). The ovary is oblong in shape and measures 4.2 by 3.1 by 1.1 cm. Its outer surface is uneven, and varies from yellow to gray to pinkish-purple. It has a varying consistence. The various sections through the ovary reveal some cystic areas, the smallest of which measures 0.1 cm. and the largest 1.4 cm. These cysts have a smooth, gray lining and contain a gelatinous, mucoid material. The largest cyst has a hemorrhagic lining and a blackish-red, firm, blood clot is seen in this cyst. The intervening tissue between the cysts varies in appearance, is rather firm throughout, and is not typical ovarian stroma, but seems to be somewhat fibrous, with probably some degenerative changes. One area, 0.3 cm. in diameter, is firmer than the rest and is light-gray in color. In one pole of the ovary a fungating mass is seen which is joined by a fairly large mass, which is dissected from the ovary. This entire fungating mass is 2 cm. in diameter, grayish and somewhat firm. Cut section reveals areas of brownish-red discoloration on a yellow surface.

Microscopic examination shows the mass connected with the ovary to be a neoplasm composed of epithelial cells, which for the most part are undifferentiated. The tumor is very cellular and in most places has a very delicate stroma. It is very vascular and contains numerous, very thin-walled, large blood channels. In some places where there are bands and streaks of stroma, the central part of the masses of tumor cells has degenerated, and this gives the appearance of a pseudopapillary arrangement about the stroma strands.

The tumor cells' nuclei are quite variable in size and shape, but most are large and have relatively little cytoplasm about them. Mitoses are numerous in places. The nuclei are not hyperchromatic, but have a loose, vesicular appearance. Nucleoli are small and inconspicuous when seen. There are scattered, multinuclear, tumor giant cells, although this is difficult to be sure of because the cell walls are indefinite everywhere. The appearance is almost that of a syncytium. This is accentuated by the fact that in many places the tumor cells have markedly vacuolated cytoplasm. In many of the clumps of cells, this vacuolization proceeds to a stage where there is a central empty area with tumor cells about it, giving the appearance of a pseudoalveolus. Floating in this central zone are often one or several tumor cells with slightly pyknotic nuclei and foamy cytoplasm. This is especially true where the central zone is very large and not empty but filled with a lacy, reticular, faintly staining material.

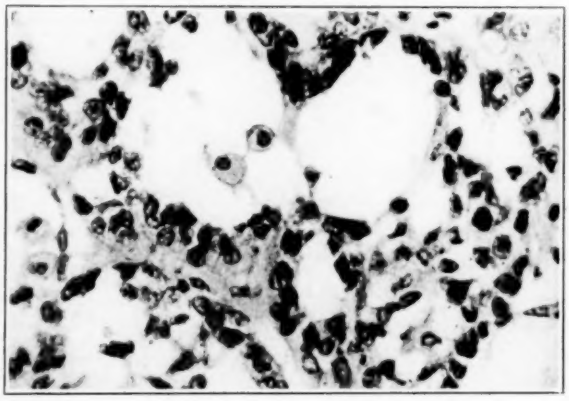

FIG. 2. High power, showing the irregularity of size and shape of the nuclei and of the tumor cells. Several mitotic figures are seen. The indefinite cell walls are obvious. Several pseudoalveoli, one containing two degenerating vacuolated tumor cells, are present. 350×.

In other places the tumor cell nests are more compact; the nuclei are more uniform in appearance, but still the cells are very anaplastic.

Where tumor and ovary are seen together, there is no hint of a capsule about the tumor, and nests of tumor cells can be seen invading the ovarian tissue. Also in some of the broader bands of stroma in the tumor, recognizable ovarian structures, such as small follicles and egg cells, can be noted.

The ovarian tissue in general is very edematous and shows a considerable number of ova and some large patches of fibrosis, resembling corpora albicantia.

Diagnosis: carcinoma simplex of ovary.

The immediate postoperative course was uneventful, and the patient left the hospital on the ninth postoperative day.

On January 22, the eleventh postoperative day, films were taken of the lungs, heart, kidneys, ureters, bladder, abdomen, lumbosacral spine, pelvis and hips. No abnormal shadows were found in any of these areas.

On the same date, she received her first exposure of deep x-ray radiation, followed by a subsequent course of seventeen exposures. She had some reaction to the treatments. Also, during the course of treatment, the incision spread slightly. One week after the last treatment, she weighed 87 lb. and had a hemoglobin of 65 per cent (Tallqvist).

On May 4, 4 months postoperatively, and after a high-caloric, high-calcium diet, with heavy doses of iron, her weight was 94 lb. and hemoglobin 75 per cent. The abdominal wound was well healed. Rectal examination disclosed no abnormalities. On October 5, the patient stated that she had felt "fine" since her last visit. She weighed 102 lb. The rectal and abdominal examinations disclosed no abnormalities. A number of follow-up visits were then made by her, and on April 24, 1937, 15 months postoperatively, the findings were unchanged, even to the extent that the menstrual periods had not been established.

Time will tell what the future holds in store for this patient. In view of the fact that there is a dearth of contributions in the literature for this type of case, it is difficult to ascertain what has happened in similar cases and so be partially guided by them. The fact that the ovary was found ruptured and that blood was free in the pelvis would incline one to give an unfavorable prognosis. However, this is contradicted by the experience of others, for we find the following statement by Meigs:[12] "Great care should be taken not to rupture any ovarian cyst or tumor as it is being removed. Although in a series of ovarian tumors at the Massachusetts General Hospital good results were found in those that had been ruptured, it is definitely better not to allow rupture and spilling of the malignant contents in the abdomen."

Of course the prognosis is much more favorable than otherwise since the left ovary was extremely small, firm, and appeared normal. One would expect to find metastases there almost as early as in any other part of the body. Another factor toward a favorable prognosis is that radiation was begun early, eleven days after the operation. This contention is borne out by the following excerpt from a paper written by McNamara et al.:[7] "The malignant tumors of the ovary metastasize to regional lymph nodes, the peritoneal cavity, the abdominal organs, and the lungs. All authorities agree that a cure demands early extirpation. This should be followed by roentgenotherapy. The neoplastic cells are of an embryonic type and are susceptible to the x-rays." Burnam[11] writes: "If a malignant tumor of the ovary is completely removed and has not broken through the capsule, there is no indication in the present state of our technical knowledge and development for postoperative radium or x-ray treatment. On the other hand, in inoperable growths and where growths have metastasized to the peritoneum and where they are causing ascites or pressure, the results observed in the way of palliation and occasional cure more than justify an effort at postoperative radiation. Indeed, some of the very malignant tumors of the ovary, and especially those occurring in young girls, are very radiosensitive."

Gardner[13] writes: "It is becoming more apparent each year that the microscope, not the naked eye, is the all-essential instrument in the differential diagnosis of ovarian lesions." In this respect, I am indebted to Drs. Olga Leary, Harold E. MacMahon, Joe V. Meigs and M. J. Schlesinger of Boston, and Francis C. Wood, F. M. Smith and John Boyd, of New York, for their interest in studying the pathological slides in this case. The diagnoses made by them in the main concurred, for the majority agreed that the tissue was that of a "rapidly growing, undifferentiated carcinoma of the ovary"; several, however, were inclined to call the tumor a "folliculoma." These differences of opinion created much pathological discussion, because prognosis depended in great part on the diagnosis.

At present, seventeen months after the operation, the patient has shown steady improvement. During the first five months following the operation she had very occasional attacks of abdominal pain. Recent physical examination, however, disclosed no abnormal changes. The patient has improved in general health, has gained weight, and has continued with her daily school work and physical activities.

SUMMARY

1. The case of a thirteen-year-old female child, upon whom an operation was performed with the finding of a ruptured right ovarian tumor, is reported.

2. Various pathologists concurred in a diagnosis of "rapidly growing carcinoma of the ovary," and in addition, the specific diagnoses of "carcinoma simplex" and "folliculoma" were made.

3. Statistical data are offered attesting to the rarity of carcinoma of the ovary developing in the young female.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 23401

PRESENTATION OF CASE

A fifty-seven-year-old American housewife was admitted complaining of hematuria.

About four years before entry the patient, who had previously been well, developed a very severe, constant, nonradiating pain in the right flank. Associated with this discomfort there was increased urinary frequency. The urine was blood tinged, but there was no dysuria. A hypodermic injection was necessary to produce relief from the pain. A few days later, following a cystoscopy, she was advised to have her right kidney removed. Since the pain had subsided and there was only slight residual tenderness in the flank, the patient decided not to be operated upon. During the succeeding three and a half years there were attacks of colicky pain occurring about once or twice each month. The pain appeared in the right flank, radiated down into the right lower quadrant and suprapubic region, and then abated. Associated with these attacks the patient noted the passage of small flecks of blood in her urine. During the six months preceding her admission to the hospital the attacks became more frequent but were not increased in severity. Three days prior to entry, pain occurred in the right flank and rapidly became very severe. The discomfort was constant, and urinary frequency became evident. On the following day there was pronounced malaise, and she noted nausea and fever. The urine gradually became bloody in character. Shortly before coming to the hospital she began to vomit repeatedly, and the flank pain was sufficiently severe to require morphine for relief.

The past and family histories were noncontributory.

Physical examination showed an obese woman lying quietly in bed in no evident discomfort. The lungs were clear. The heart was normal. The blood pressure was 120 systolic, 80 diastolic. There was tenderness in the right upper quadrant, flank and costovertebral angle. The right kidney could be palpated and was tender.

The temperature was 100°F., the pulse 90. The respirations were 25.

Examination of the urine showed a specific gravity of 1.030 with a trace of albumin and a brown precipitate with the Benedict test. The sediment contained many red blood cells, and there were 40 to 50 white blood cells per high-power field. A fasting blood sugar was 384 mg. per cent, and the CO_2 combining power was 51 vol. per cent. The nonprotein nitrogen of the blood was 24 mg. per cent. A white blood cell count was 17,100.

A plain x-ray film of the abdomen demonstrated a normal left kidney. The right kidney was not well seen but appeared to be enlarged. There was an area of calcification overlying the right transverse process of the fifth lumbar vertebra. An intravenous pyelogram showed normal filling of the left kidney pelvis, calices and ureter. There was no function on the right side, and the kidney outline was not well seen. After insertion of a catheter into the right ureter the area of calcification could not be found. A small amount of dye was observed lying adjacent to the catheter in the ureter at the level of the fifth lumbar vertebra.

The cystoscopy done at the time of the pyelogram showed only cloudy, purulent urine in the bladder. The catheter passed up the right ureter easily, but drainage was poor. The patient was treated palliatively during the next week, and her diabetes was controlled. There was no record of further pain, and her temperature became normal. On the eleventh hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. GEORGE G. SMITH: We have a history of four years' duration, the outstanding symptom having been that of pain in the right flank with frequent attacks of right renal colic. There was hematuria, massive at first but later on characterized by only small flecks of blood. There was frequency of urination. The significance of that frequency without dysuria in a case of this sort I think is doubtful. It is known that abscesses in the kidney may produce frequent urination, simply by reflex action, without there being any disease in the bladder at all. Apparently the patient did not have anuria and fever until just before she entered the hospital. It sounds as if it were a chronic condition, since her difficulties had lasted four years. However, her condition suddenly became worse, and to it was added the factor of infection, which caused her fever.

What are the possibilities that we have in mind as we read the history? The first thing one thinks of is renal stone. Tuberculosis of the kidney, with more or less obstruction of the ureter causing retention in the kidney, is a possibility, although not so strong a one as stone. Tumor of the kidney or ureter would, of course, be in one's mind on account of the hematuria. Pain may or may not be present with tumor in the kidney. Unfortunate-

ly in many cases it is not present; that is why patients go so long with large tumors before they come to treatment. But it is possible to have obstruction with a malignant kidney and also a complicating element of infection, so that the patient may have a good deal of pain. The tumor, particularly if it is of the pelvic type, may obstruct the outlet from the kidney pelvis so that the patient has infection within the pelvis. It would seem unlikely that tumor of the kidney was present in this case for the patient apparently had a normal functioning kidney, except for passing a slight amount of blood, for a period of four years. One would think that in that time something more definite would have happened if a tumor had been present. The chronicity of the symptoms, without marked change, makes one think more strongly of tuberculosis.

We add to our knowledge, gleaned from the history, the fact that the right kidney was large and tender on physical examination. The increase in size might be due to tumor in the right kidney, although a tumor is usually not tender. I should think that the tenderness was more suggestive of an inflammatory process, either tuberculosis or a chronic infection of some sort. Hydronephrosis is another possibility which perhaps I should have mentioned as one of the causes of bleeding, although bleeding is not an outstanding symptom. Primary hydronephrosis would hardly be likely to give a history of this sort.

At entrance the temperature was 100°F., the pulse 80, and the respirations 25. Examination of the urine showed a specific gravity of 1.030. The nonprotein nitrogen was 24 mg. per cent. That is interesting because it suggests that the other kidney is perfectly normal and able to do good work. Generally speaking it is only when both kidneys are diseased that one finds an elevation of the nonprotein nitrogen. Of course, it is obvious that she was a severe diabetic.

There is no mention of stone in the kidney on x-ray examination, so it is fair to assume that no shadows were seen in that kidney.

X-Ray Interpretation

Dr. George W. Holmes: It is true that there is no shadow suggesting stone within the kidney, but I must say this other shadow, the one described as calcification overlying the right transverse process of the fifth lumbar vertebra, looks a good deal like a stone in the ureter, although the long axis is a little unusual for the ordinary course of the ureter. This retrograde pyelogram shows large masses of opacity in the region of the right kidney. As was mentioned, the other shadow has disappeared. Whether or not it is this dark area within the injection fluid, I am not sure. If it is, it suggests that it is really included in the ureter; and if so, a catheter passes to it. One would think that if the trouble were due to a stone in the ureter which the patient had had for four years the catheter would have difficulty passing it, and there would be much more dilatation of the ureter above the stone. I should interpret the appearance as being due to marked hydronephrosis. The kidney is apparently destroyed.

Dr. Smith: I should agree with the radiologist's report, as given in the summary, that the shadow had disappeared.

Dr. Holmes: Let us compare the position of the ureter with the position of the shadow. The position of the ureter is unusual. It is farther out than one would expect and corresponds fairly well with the position of the shadow. Then, the fact that the shadow disappeared in the retrograde pyelogram makes me think it was more likely to be in the ureter than somewhere else.

Differential Diagnosis (Continued)

Dr. Smith: On the basis of the facts as we know them now, what are the outstanding possibilities? The question of a tumor is still present. We have no good evidence to rule it in or out. The question of tuberculosis is still present. If the catheter had gone up the ureter with a good deal more difficulty, I think I should have suspected tuberculosis more. Also, the fact that this ureter is pretty smooth, although slightly dilated, is not what one would expect in long-standing tuberculosis, in which the ureter is usually involved down to the bladder, but one cannot rule out tuberculosis because the ureter is not involved. There may be a nonopaque stone blocking the kidney outlet. There may be this stone in the ureter which Dr. Holmes speaks of; but to me it seems difficult to see, though in that one film the shadow is very suggestive.

Dr. Holmes: In the one with the catheter, before they injected, I cannot find any stone. That is hard to explain.

Dr. Smith: We have, then, a nonfunctioning, enlarged, tender, infected kidney. Is it infected tumor, is it tuberculosis, or is it pyogenic infection on top of stone? I think these are the outstanding possibilities. Hydronephrosis is unlikely; it is a possibility, however, but a rather remote one. I should guess, and that is all one can do on the evidence that we have, that this is tuberculosis. I think the patient undoubtedly has a pyonephrosis, probably tuberculous.

Preoperative Diagnosis

Right hydronephrosis.

Dr. George G. Smith's Diagnosis

Tuberculosis of the kidney.

Anatomic Diagnosis

Papillary carcinoma of the renal pelvis and ureter.

Pathological Discussion

Dr. Tracy B. Mallory: The kidney which was cut down on was obviously enlarged. It was resected and opened in the operating room, and a shaggy papillary mass of tumor was found in a portion of the pelvis. The remainder of the pelvis was somewhat dilated—enough to call it a minor degree of hydronephrosis. A frozen section was done at that time and confirmed the gross diagnosis of papillary carcinoma. On the strength of that report, the surgeon went back and resected 10 cm. of the ureter, in the upper 3 cm. of which he found a focus of similar papillary tumor.

I think that explains why you were correct in assuming that the catheter did not go all the way up to the pelvis. It came up against the papillary tumor in the ureter itself and could go no farther. A tumor of this sort, of four years' duration, I think one might reasonably have expected to extend much farther down the ureter. It is characteristic of them to involve eventually the entire ureter and even portions of the bladder.

A Physician: Is that not a long duration for a process of this kind? Was it quite a low-grade malignancy?

Dr. Mallory: Not so low a grade as I would have expected, in view of the duration. It may have begun to grow more rapidly, however, within the last year. Many of these papillary tumors of the renal pelvis are almost identical in histology with those in the bladder. The pelvis is, of course, lined with the same type of transitional epithelium, and a great many of the tumors arising in both places are histologically benign in appearance but clinically malignant. However, from the histologic point of view as well, I think one would have to classify this case as malignant.

Dr. Ross Mintz: I think it would be interesting to know what diagnosis they made three and a half years before, when they advised her to have her kidney out.

Dr. Mallory: That was done in another hospital. No attempt was made to find that out.

A Physician: Was any attempt made to find a stone in the ureter?

Dr. Mallory: They found none, and since they removed 10 cm. of the ureter, which would have included the area under suspicion, I do not believe there was any.

Dr. Barney: I should think, looking at the plates, and even with the history to help me, that a diagnosis of intrapelvic disease would be almost the last thing one would think of. It is a very unusual x-ray picture.

Dr. Colby: She must have had more bleeding, because such tumors always bleed a great deal.

Dr. Mallory: She had red cells in the sediment at all times, although apparently not very much in the way of gross hematuria.

CASE 23402

Presentation of Case

A forty-six-year-old American shopkeeper was admitted complaining of weakness and shortness of breath.

The patient was well until two and a half years before entry, at which time he first noted swelling of his feet and ankles. This occurred while he was playing baseball, and on the night of onset both feet became hot and tender. He felt very weak, feverish and miserable. The tender swelling persisted and the patient had arches fitted in order to get about. Two weeks after the onset a physician was consulted, and the patient was put to bed for about one month. During this period he developed similar painful swellings in both hands and wrists, but his general condition improved. For a year following the onset the patient was troubled with frequent though transient attacks of painful swelling in the wrist, ankle and knee joints. He was unable to work during this period and spent most of the time in bed. Subsequently his condition improved, and the joint symptoms subsided. He returned to work and remained well until six months before coming to the hospital. At this time he first noted dyspnea when climbing stairs. This symptom progressed very rapidly until he became unable to walk on level ground without developing shortness of breath. There was associated fatigability, weakness and malaise. Five months prior to entry he went to bed for a period of four weeks, and edema which had appeared in his lower extremities partially subsided. It recurred directly he arose, however, and the dyspnea persisted unabated. About two months before admission the patient developed blurring of vision and rather severe generalized headache. He was again confined to bed but the symptoms remained unimproved. Orthopnea appeared, and although the administration of digitalis caused some diminution of the edema, the respiratory discomfort continued.

The past history was noncontributory.

Physical examination showed a well-developed and nourished middle-aged man propped up in

bed, breathing with difficulty and perspiring slightly. The pupils were equal and reacted normally to light. The fundi exhibited numerous fresh flame-shaped hemorrhages and patches of yellowish exudate. The arterioles were markedly tortuous. The chest was barrel-shaped, and dulness was elicited at both bases posteriorly up to the angles of the scapulae and anteriorly on the right side up to the third rib. Breath sounds were diminished in intensity in the areas of dulness, but in the upper portions of both sides of the chest they were bronchovesicular to bronchial in character. Numerous coarse moist rales were generally audible. The heart was considerably enlarged to the left, and there was a gallop rhythm with pulsus alternans. A rather harsh apical systolic murmur was heard. The blood pressure was 270 systolic, 160 diastolic. Abdominal examination was unsatisfactory because of the patient's upright position, but there was slight resistance in the right upper quadrant, and the liver extended three fingerbreadths beneath the costal margin. There was slight edema of the lower extremities up to the knees.

The temperature was 100°F., the pulse 110. The respirations were 34.

Examination of the urine showed a specific gravity of 1.024 with a large trace of albumin. The sediment contained six red blood cells and two white blood cells per high-power field. The blood showed a red cell count of 4,500,000 with a hemoglobin of 80 per cent. The white cell count was 14,700, 74 per cent polymorphonuclears. Examination of the stools was negative. A blood Hinton test was negative. The nonprotein nitrogen of the blood was 61 mg. per cent. The uric acid was 7.2 mg. per cent, and the chlorides were equivalent to 111 mg. N/10 sodium chloride. The serum protein was 6.4 gm. per cent.

On the day following entry 1,770 cc. of fluid was removed from the left chest, and on the next day 1,560 cc. was removed from the right. The fluid exhibited a specific gravity of 1.012 and clotted after standing. Following the thoracenteses the patient appeared to improve slightly, but the nonprotein nitrogen of the blood gradually rose to 105 mg. per cent. On the fourth hospital day he became semistuporous and exhibited Cheyne-Stokes respirations. On the following day he had convulsive tremors, and died shortly afterward.

Differential Diagnosis

Dr. John H. Talbott: This is a forty-six-year-old American shopkeeper who came in complaining of cardiac symptoms with an interesting story of polyarthritis two and a half years before. Apparently he was perfectly normal up to then as he was able to play baseball the day of onset of joint symptoms. The joints of his feet and ankles became hot and tender, and the swelling persisted until a physician advised him to go to bed, where he remained for about a month. While in bed he had migratory polyarthritis with involvement of the hands and wrists. During the next year the patient had a continuous polyarthritis which incapacitated him for work His condition improved, however, and for a period of about a year he was able to work. Six months before coming to the hospital he had dyspnea which progressed very rapidly. During the remainder of the history there is no mention made of joint disease.

I think there are at least four types of arthritis that should be considered. Migratory polyarthritis from rheumatic fever is unusual at this age. The symptoms could be explained on the basis of rheumatoid arthritis, but with this long history we would expect on physical examination more evidence of joint involvement. Gonococcus arthritis is another possibility, and we should like a negative history of exposure as well as a negative complement fixation test. The other joint disease which would fit in with the remainder of the story is gout. The onset of acute arthritis in a man at the age of forty-six is perfectly consistent with a diagnosis of gout. The complete recovery and disappearance of symptoms during a year's interval before the final admission is more like a condition associated with gout than with any other joint disease.

Let us now return to the present illness. Following the onset of dyspnea the patient was in bed for about four weeks with edema of the lower extremities. Two months before admission he developed blurring of vision and generalized headaches, which make us think of hypertensive renal disease. The patient became orthopneic, and although digitalis helped to a certain extent, it was advisable to bring him to the hospital. A noncontributory past history is against this being rheumatic fever. We should like to know whether there was a family history of arthritis or gout, but presumably there was not.

Physical examination showed flame-shaped hemorrhages and patches of exudate in the fundi, with tortuous arteries. There was evidence of fluid in both pleural cavities and enlargement of the left ventricle of the heart. The gallop rhythm with pulsus alternans suggests a badly damaged myocardium. The apical systolic murmur indicates insufficiency of the mitral valve, probably from chronic dilatation. The liver was enlarged. The absence of hyperpyrexia is against this being subacute bacterial endocarditis. The increased respiratory rate is probably unrelated to the bilateral pleural effusion.

Examination of the urine showed a specific gravity of 1.024, with a large trace of albumin. This normal specific gravity was observed at repeated examinations and is inconsistent with the other findings. The sediment contained red and white blood cells and casts. There was no evidence of anemia from examination of the blood. The negative Hinton test helps us exclude syphilitic heart disease. The nonprotein nitrogen of the blood was 61 mg., and the uric acid 7.2 mg. per cent. In the main there are only two conditions outside of gout which give an elevated uric acid. These are renal insufficiency and leukemia. I see no evidence for seriously considering leukemia. There obviously is renal insufficiency whether primary or secondary to gout is not clear. An elevated uric acid of 7.2 mg. is certainly higher than we would expect with a nonprotein nitrogen of only 61 mg. The concentration of serum chlorides of 111 milliequivalents per liter is in favor of a tubular nephritis. However, from clinical examination only, one cannot predict pathologic changes in the kidneys, or chemical changes in the blood, in many cases of renal insufficiency. The normal serum protein is against its being a so-called nephrosis.

On the day following entry, fluid, which had a specific gravity of 1.012 and clotted after standing, was removed from both chests. This is evidence of an exudate probably from a failing heart. The patient died on the fifth hospital day with convulsions.

In summary of this case I should like to connect the past history of polyarthritis with the present exitus. Acute rheumatic fever two years before with terminal myocardial failure could account for many of these symptoms, but the age of the patient and the degree of renal involvement are much against this diagnosis. If acute gout were the principal disease beginning two and a half years ago we should expect a nephritis of the vascular type if it were to be explained on one diagnosis. We do not have enough evidence, however, to make a diagnosis of gout. My diagnoses, then, are vascular nephritis, hypertensive heart disease with chronic myocarditis, bilateral pleural effusion and a question of gout. It may be that the arthritis will not be explained satisfactorily even on pathological examination.

Clinical Diagnoses

Hypertension.
Uremia.

Dr. John H. Talbott's Diagnoses

Vascular nephritis.
Hypertensive heart disease with chronic myocarditis.
Pleural effusion, bilateral.
Gout?

Anatomic Diagnoses

Chronic vascular nephritis.
(Uremia.)
Cardiac hypertrophy, hypertensive type.
Pericarditis, acute fibrinous.
Hydrothorax, bilateral.
Rheumatic myocarditis.
Arteriosclerosis: minimal, aortic; moderate, coronary.

Pathological Discussion

Dr. Benjamin Castleman: The autopsy on this man showed that death was due to a severe vascular nephritis. The kidneys weighed 275 gm. and were quite granular. Microscopically almost every glomerulus showed some degree of hyalinization, few being completely destroyed, but the majority exhibiting marked capillary thickening. The arteriolar sclerosis in some places was severe enough to produce luminal occlusion. There was also a moderate degree of arteriolar sclerosis in the spleen and pancreas. The heart weighed 600 gm. and grossly was quite consistent with the hypertensive type of hypertrophy. There were no valvular lesions. Microscopically, however, in between many of the muscle bundles and especially around the smaller coronary vessels there were collections of monocytes, many multinucleated, distributed in a collagenous meshwork. These are quite consistent with the Aschoff bodies that are found in rheumatic fever and would favor the idea that the polyarthritis was rheumatic in origin. I do not believe that these lesions are ever seen in gout. There was also a terminal acute fibrinous pericarditis, such as is so often seen in uremia. There is no doubt that the patient died of his renal insufficiency. I think that the rheumatic myocarditis had little to do with his death.

The New England
Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
The New Hampshire Medical Society
The Vermont State Medical Society

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Subscription Terms: $6.00 per year in advance, postage paid, for the United States; Canada, $7.04 per year; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Saturday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the New England Journal of Medicine, 8 Fenway, Boston, Mass.

HOSPITAL-CARE INSURANCE

Group hospital-care insurance is a logical way of limiting the economic hazard of severe illness. The uneven distribution of the costs of such illness is clearly described in *The Final Report of the Committee on the Costs of Medical Care*.[1] This analysis indicates that, although but one person in seventeen receives hospital care per year, illnesses which involve hospitalization are responsible for 50 per cent of the total yearly charges for medical care. Roughly half of such costs are hospital expenditures. For many families bills thus incurred are catastrophic, and one readily appreciates why patients in the large hospitals in Boston, even prior to 1930, paid but 25 per cent of the cost of their hospital care and became charity patients who paid little or nothing for physicians' services. To quote from the report:

> The individual family derives no comfort from the knowledge that the *average* cost of medical care is not excessive for families with the *average* income. If a family lays aside for medical costs 4 per cent of its annual income (say $110), it may spend only $10 or it may spend $1,000. . . . The unpredictable nature of sickness and the wide range of professional charges for nominally similar services render budgeting for medical care on an individual family basis impracticable. . . . It is impossible for 99 per cent of the families to set aside any reasonable sum of money with positive assurance that that sum will purchase all needed medical care.

* * * * *

Group hospital insurance was introduced by the Baylor University Hospital in Dallas, Texas, in 1929. The growth of such groups demonstrated that the American people were interested in limiting the economic hazard of hospitalization. By 1932 the advantage of co-operation instead of cut-throat competition among the hospitals was appreciated and city-wide, free-choice, nonprofit plans began to make their appearance.

The movement toward budgeting hospital charges in this country differs from what superficially appears as a similar trend in Europe. The health insurance programs of Europe are primarily for people with very low incomes or for charity patients. The insurance premiums are intended to cover only a portion of the expenses, and the balance is made up by taxation. In America the objective is not to care for the charity patient but is rather to make it possible for employed persons to receive the facilities provided by hospital care by budgeting a moderate yearly charge and thus to avoid the risk of financial embarrassment from incurring hospital bills that cannot be paid. The cost of the insurance against this risk is sufficient to provide funds for the actual cost of hospital care, the administrative expenses, and the establishment of such reserves as will ensure the financial stability of the incorporated service. The steady development of the movement in this country largely reflects the conservative manner in which it has been guided by the American Hospital Association. At present there are thirty-seven nonprofit, free-choice, hospital service corporations operating throughout the country with an enrollment of over

a million subscribers. No such service once started has ever been discontinued or failed to meet its obligations to subscribers or hospitals. The Associated Hospital Service Corporation of Massachusetts, which has just started to operate, as described elsewhere in this issue of the *Journal,* already has forty-one member hospitals throughout the state, nineteen of which are located within the metropolitan district of Boston.

* * * * *

The American Hospital Association's committee on hospital service has published *An Historical and Critical Analysis of the Periodic Payment Plan for the Purchase of Hospital Care.*[2] Physicians should read this that they may be familiar with the movement. For here is an adjunct to the organization of our medical services in which physicians have a major place. The subscriber to a hospital-care insurance plan is admitted to the hospital only upon recommendation of a physician and during hospitalization is under the care of his own physician. Thus utilization of the service not only is controlled by the family physician, but the quality of the medical care and benefit to the subscriber are also largely prescribed by the qualifications of the physician. Moreover, the evidence already at hand indicates that the reduction of hospital costs under the service permits many patients, who otherwise would demand free care, to pay reasonable fees to physicians during hospitalization. Finally, a service that provides the much needed extension of hospital facilities to a large portion of the public and at the same time brings financial support to our hospitals from the public they serve should command the support of the medical profession.

Problems will doubtless arise. But in the first flush of enthusiasm we foresee more of the public receiving the benefits of hospital care, ward patients becoming semiprivate patients, and semiprivate patients turning to private patients, while doctors, nurses and hospitals derive an income from patients who heretofore constituted a public charge. And all this will be accomplished at the expense of the individuals who can rejoice in the economy of good health and look forward with a minimum of anxiety to their day of serious illness.

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2. Rorem, C. Rufus: An Historical and Critical Analysis of the Periodic Payment Plan for the Purchase of Hospital Care. Chicago: American Hospital Association, 1937.

GEOGRAPHICAL DISTRIBUTION OF MORTALITY

The United States Public Health service has published an interesting report (June 18, 1937) on the regional distribution of deaths from tuberculosis, cancer, appendicitis and typhoid fever, confining its study, for obvious reasons, to the white population.

Except for the four states—Nevada, Arizona, Colorado and New Mexico—where tuberculous patients customarily go for treatment, the belt of highest mortality runs through the New England states, as far south as the Virginias, Kentucky and Tennessee, and west and south to Missouri and Arkansas.

The cancer belt, if it may be so called, includes New England and the Middle Western states, excluding the South and the Northwest, except for Washington and Oregon, and runs down the Pacific coast through California. The regional distribution of cancer mortality, even including such factors as inadequate hospitalization and diagnostic facilities, remains unexplained and presents an important field for intensive surveys of medical service and for intensive epidemiologic studies of environmental, familial, dietary, industrial and other conditions.

The highest appendicitis death rate occurs in the Rocky Mountain section from Montana as far south as New Mexico, and includes South Dakota, Nebraska, Kansas and Iowa; and its distribution, with a consistent decrease in the recorded death rate both eastward and westward from the Rocky Mountain region, suggests at least the possibility of the operation of some geologic or climatic factors upon the incidence of the disease.

The typhoid fever belt is largely in the basin of the Mississippi River and its tributaries and includes, by and large, the majority of the Southern

states as far west as New Mexico and Arizona. This mortality may be largely, if not entirely, explicable by regional and local differences in the application of general sanitary measures and in climatic and soil conditions, although the possibility is admitted that there are factors in the causation of this disease which are not yet known.

It is concluded that the regional distributions of mortality, and inferentially of morbidity, from all these unrelated diseases are not yet satisfactorily explicable and present important fields for detailed survey of medical service and for practical epidemiologic studies on a broad scale.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY

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Case History No. 40. Bleeding at Six Months

Mrs. L. F., a white primipara, aged thirty-seven years, entered the hospital December 23, 1931, complaining of vaginal bleeding. Her last period started on June 1. On admission the patient reported a slight stain the previous evening; there was no pain or discomfort. On arising in the morning she noticed another slight stain, her abdomen felt sore, and she was having occasional cramps. She was sent to the hospital immediately.

The family history was not remarkable. There was no history of scarlet fever, diphtheria, tuberculosis or other illnesses, or of surgical operations. Her periods had always been regular. She had been married for ten years, but had never before been pregnant, though wanting a baby. On examination two weeks previous to entry the heart and lungs were essentially negative. The breasts were normal, and the position of the fetus was not made out. The presenting part was floating. The fetal heart tones were of good quality. Vaginal examination showed the presenting part high, the cervix soft, and the vaults free of masses.

Physical examination on admission revealed a very slight stain of bright blood. The uterus was much larger than expected for her dates and quite stiff in consistence. The patient was distinctly uncomfortable although she was having no definite uterine contractions. No fetal heart tones or motion was made out. The cervix was not dilated or taken up. A diagnosis of premature separation of placenta was made.

The red blood-cell count was 4,000,000; the hemoglobin, 70 per cent; and the blood pressure, systolic 140, diastolic 80. The urine was essentially negative.

The patient was taken to the operating room, and under general anesthesia the abdomen was opened in the midline. The abdomen was filled with yellow fluid, and the uterus had a definite bluish tinge. The uterus was opened in the midline, and the fetus and placenta were found lying free in the uterine cavity. No clots were present in the uterus. The fetus and the placenta were removed, the former showing early signs of maceration. The uterus shut down well, seemed to have good tone, and the color improved. It was closed in three layers. The abdomen was closed in three layers, and the patient was in good condition after the operation.

The patient remained in the hospital for fifteen days after which she was sent home. Postpartum examination February 1, 1932, showed the uterus of normal size, in good position, and the vaults free of masses. The cervix was smooth, the perineum firm, and the breasts of normal appearance.

In summary, a thirty-seven-year-old primipara had an uneventful pregnancy up to six months at which point without warning she had complete separation of the placenta. At no time did she have symptoms of toxemia. Her blood pressure was essentially normal. A classical cesarean was done. The patient was never seriously sick and made an excellent recovery.

Comment. This is one of those unexplained cases of separated placenta. There undoubtedly was some retroplacental hemorrhage although no free blood was found in the uterus. The fact of the patient's age and long married life without pregnancy, although wanting children, points to a low fertility. This made possible a poorly growing placenta which did not invade sufficiently for a firm attachment. This, however, is theoretical, and there was no demonstrable cause for this accident.

In regard to the method of treatment it could be argued that delivery from below might have been preferable. With a dead baby and a six months' pregnancy a Spanish windlass could have been applied, the vagina firmly packed, and the patient allowed to go into labor. The reasons for cesarean section in this case were as follows: a long, hard undilated cervix in an elderly primipara and the acute total separation which indicated hemorrhage of considerable amount into the uterine wall.

A series of selected case histories by members of the section will be published weekly.

Comments and questions by subscribers are solicited and will be discussed by members of the section.

MISCELLANY

ASSOCIATED HOSPITAL SERVICE CORPORATION

Because of their importance to the future of the medical profession in general and of the practitioner in particular, the following letter and enclosure, which were recently sent to all practicing physicians in Massachusetts, are reprinted in full. No physician, in fairness to his patients, his profession and himself, should neglect to familiarize himself with the details of service offered by the Associated Hospital Service Corporation.

* * *

To Members of the Massachusetts Medical Society and Other Physicians throughout the Commonwealth:

In the interest of the Associated Hospital Service Corporation of Massachusetts, I should like to call to your attention the following facts about the corporation:

Enabling legislation for the formation of the Associated Hospital Service Corporation of Massachusetts was enacted at the 1936 term of the State Legislature. The passage of this act, or amendment, had the support of the Commissioner of Insurance and the Commissioner of Public Welfare. The enabling act contains provision for approval of all contracts and rates by both the Commissioners of Insurance and of Public Welfare, as safeguards for all concerned.

The Council of the Massachusetts Medical Society approved in principle a group hospitalization plan for the State at its meeting in Springfield in 1936. Conferences on the subject were continued, and the final form of the contract upon which to initiate this service was evolved.

Various medical societies, and other organizations throughout the Commonwealth, elect directors and direct the policy of the corporation. The Hospital Council of Boston, the Massachusetts Hospital Association, the Massachusetts Medical Society, Suffolk District Medical Society, Middlesex East District Medical Society, Middlesex South District Medical Society, Norfolk District Medical Society, and the Boston Council of Social Agencies have voting power. Other organizations in the State will be invited to appoint voting members.

You will note in the following bulletin that Associated Hospital Service in *no way* interferes in the relation between the subscriber patient and his physician. I believe that this plan is a constructive step toward eliminating compulsory sickness insurance, which many people favor.

The medical profession can be of material assistance in establishing this nonprofit public service if all members will learn about group hospitalization and be in a position to answer the questions of their patients. I urge you to read this bulletin carefully and to seek explanation from the Executive Director, or from a member of the Board of Directors, regarding features of the plan which you do not understand.

Very truly yours,

CHANNING FROTHINGHAM, M.D., *President,*
Massachusetts Medical Society.

* * *

THE RELATION OF MASSACHUSETTS PHYSICIANS AND SURGEONS TO ASSOCIATED HOSPITAL SERVICE CORPORATION

Associated Hospital Service Corporation of Massachusetts has been organized as a group hospitalization plan to serve the entire State. It is the result of three years of co-operative effort on the part of medical societies, hospital associations, individual physicians and public-spirited citizens throughout the State.

To aid in spreading a clear interpretation of this movement, the interest and assistance of the medical profession is essential. Therefore, this pamphlet is addressed to the physicians and surgeons of Massachusetts, whose earnest co-operation is sought in making known to the public the benefits of membership in the Associated Hospital Service Corporation.

One of the purposes of this service is to ensure adequate care for the sick with fair remuneration to member hospitals for services rendered. This will lessen the charitable load, carried of necessity by many hospitals. It will also bring the services of hospitals within easier reach of the public, and in general facilitate the practice of medicine.

This group hospitalization plan was organized as a public service to operate without profit and without charity. In the many cities where similar plans are in effect, a service of great benefit has been rendered.

In the United States during the past six years more than one million persons have become subscribers to the more than seventy services in operation in as many cities. New York City alone has a half million subscribers. It is generally agreed that the hospital service plan is a constructive step toward meeting the high cost of illness.

Illness which involves both a hospital bill and a doctor's bill is often more of a burden than the average person is prepared to meet. Persons in such circumstances have become easy prey to loan sharks, have found it necessary to mortgage future income, or else try to solve the problem by going into hospital wards where they pay only a hospital bill, perhaps only a part of it, and also receive free medical service. Many persons who now depend upon ward service (because they cannot pay the bills of both hospital and attending physician) would prefer to pay for their medical service in private or semiprivate accommodations.

It is impossible to budget for unexpected hospital care within any year. Group budgeting, or group hospitalization, is the only known solution.

In this plan the normal relation between the physician or surgeon and the subscriber patient is in no way disturbed. Quoting from the subscriber's contract: "This plan does not confer upon any member hospital any right to select a physician or surgeon for the subscriber. The subscriber shall be at liberty to select his physician or surgeon, provided only that such physician or surgeon is acceptable for practice in the member hospital to which the subscriber is admitted."

The contract specifically states that the subscriber shall choose his own physician or surgeon. Therefore, there can be no interference from the subscriber's employer, the hospital or this corporation.

The arrangement for the professional fee is entirely between the doctor and patient. Quoting from the contract: "Benefits hereunder do not include services of the subscriber's attending physician, surgeon, special nurses, or their board. Separate arrangements must be made with the physician, surgeon, and special nurses for the payment of their fees for services."

If a subscriber does not have a personal or family physician, and applies to a hospital for care, the hospital will recommend a list of physicians privileged to practice in that hospital, and the subscriber selects his attending physician.

If a subscriber patient is unable to pay a fee for professional services, such a patient may be admitted to ward service at the discretion and instructions of the subscriber's personal physician. (No public announcement is made of this.)

The contract between Associated Hospital Service Corporation and the subscriber leaves undisturbed the fundamental relation of doctor and patient. The physician's relation is the same as it would be to any private patient.

Associated Hospital Service Corporation benefits include:

- Bed and board in semiprivate accommodations, that is, rooms containing from one to four beds.
- Care for twenty-one days in one or more admissions in each contract year.
- Use of operating room and delivery room.
- Cost of anesthesia and the administration thereof to a maximum of $10.00 for each admission.
- Ordinary medications and dressings.
- Routine laboratory and pathological services, electrocardiograms, basal metabolism tests, and blood chemistry, when ordered by the attending physician.
- General nursing service.
- Professional services of resident staff.
- Other customary routine care.
- Care of obstetrical cases only after eleven months of continuous membership. Obstetrical care includes any condition resulting from pregnancy, the care of the mother, and ordinary nursery care of the infant during the hospital stay of the mother.

Quoting from the contract: "Hospital service will be rendered only upon authorization and recommendation of a physician who is licensed to practice medicine by the Commonwealth of Massachusetts, and is acceptable to the member hospital selected. During the period of hospitalization, the subscriber must be under the treatment and care of a physician in accordance with his staff privileges at the member hospital selected."

The benefits included cover the treatment and care of all illnesses or injuries regularly accepted for treatment by the member hospital selected, but do not cover, in any event, pulmonary tuberculosis after diagnosis as such, venereal diseases, quarantinable diseases or mental disorders.

Benefits do not include hospital care of cases provided for under the Workmen's Compensation Act.

All costs of x-ray diagnosis and treatment must be paid by the subscriber patient.

Semiprivate accommodations are regularly provided, although the patient may occupy a private room upon payment of the difference between $5.00 per diem and the hospital's daily rate for such room. Those subscribers selecting private accommodations pay directly to the hospital 50 per cent of the regular rate charged private patients for such special services as laboratory examinations, which are not usually included in the board and room rate.

The subscriber's dependents, if enrolled under the Family Plan, are eligible for hospital service, but when such dependents are hospitalized they must pay direct to the member hospital $2.00 per diem. This charge to the dependent patient is necessary because of the greatly reduced rates for family membership.

Benefits under the contract can be obtained only in Massachusetts hospitals whose applications have been accepted. In cases of accident or emergency illness, a subscriber may be hospitalized anywhere. Subscribers are admitted to a hospital and discharged therefrom only on the recommendation of their physician.

Hospital service does not include ambulatory service. The subscriber must be an inpatient to receive benefits.

When a subscriber, in the judgment of his personal physician, is in need of hospital service, such physician should arrange for the admission of the subscriber patient to a hospital. Upon arrival at the hospital, the subscriber patient should present his identification card, or receipt, which will be accepted by the admitting clerk of the hospital as authorization for admission. When admitted, the subscriber is entitled to semiprivate accommodations in rooms not exceeding four beds, and in rooms designed for semiprivate patients.

Extent and Duration of Hospital Care. Hospital service will be furnished on one or more admissions up to and including twenty-one days for each contract year during the time that each subscription agreement is in effect, provided that service thereunder is begun before the expiration date of the contract year.

Hospital service in any one contract year in excess of twenty-one days will be furnished to the subscriber by any member hospital in which treatment has begun within the twenty-one days allowed, at a discount of 25 per cent of such hospital's regular semiprivate rates.

In computing the number of days of hospital service furnished a subscriber, the day of the subscriber's admission and the day of his discharge shall be counted together as one day. If a subscriber is discharged on the same day that he is admitted, said day shall be counted as one day.

If the subscriber remains in a member hospital after he has been advised by his attending physician that further hospital care is unnecessary, whether or not the stipulated twenty-one days have been exhausted, the subscriber shall then pay to the member hospital, in cash, the full hospital charges for services received after such advice.

The benefits under any subscription agreement are entirely personal to the subscriber, and are not assignable in any way.

In cases of accident or emergency when it is impossible to move the subscriber patient to a member hospital, he may be treated where admitted, under the rules and regulations of that hospital, and payment will be made by this corporation in an amount not to exceed that paid member hospitals. The treatment furnished subscriber patients is subject to the rules and regulations of participating member hospitals, including rules and regulations governing admissions.

Hospital service is available to subscribers ten days after the effective date of the subscription agreement, except in cases of accident or emergency illness, when hospital care will be provided immediately. Such hospital service, however, does not include the treatment of conditions known to the subscriber or his physician to exist and to require hospital service on the date of the application for a subscription agreement.

Eligibility. Single individual applications cannot be accepted, because experience indicates that in order to preserve the principle of averages on which the hospital service plan is founded, it is necessary to enroll applicants in groups.

The enrollment regulations provide for the enrollment of persons employed in organizations of from five to twenty-four employees, and from twenty-five and more. Co-operation of the employer is usually necessary.

Provision is made for the enrollment of miscellaneous groups, to be composed of employed persons, but not employed in organizations of five or more persons.

The husband-and-wife membership and family membership are available at reduced rates. These two types of

membership are available only to those making remittances by payroll deduction.

The Massachusetts Medical Society, the Massachusetts Hospital Association, the Boston Hospital Council, various county medical societies, the Boston Council of Social Agencies, and outstanding physicians give Associated Hospital Service Corporation their endorsement and approval.

Officers are: president, George Putnam, member of the firm of Townsend, Anthony and Tyson; vice-president, Dr. N. W. Faxon, director of Massachusetts General Hospital; treasurer, Ingersoll Bowditch, a trustee and treasurer of Faulkner Hospital.

Directors are: Reverend Robert P. Barry, director of Catholic Charitable Bureau; Dr. J. Harper Blaisdell, official representative of the Massachusetts Medical Society; Edward Dana, president of Boston Elevated Railway Company; Dr. Channing Frothingham, president of the Massachusetts Medical Society; Louis E. Kirstein, president of Associated Jewish Philanthropies; Horace Morison, member of the executive committee of Boston Health League; and Alexander Wheeler, member of the board of managers of Children's Hospital. Roger W. Hardy is clerk of the board.

Associated Hospital Service Corporation is composed of three classes of member organizations, namely, voting members, members-at-large, and participating hospital members.

DR. WINFRED OVERHOLSER

The appointment of Dr. Winfred Overholser as superintendent of St. Elizabeth's Hospital, the government institution for mental patients in Washington, will be received as welcome news by his host of friends in New England. It is a fitting post for a man who has had wide training and who received the support of every responsible organization at the time of his failure of reappointment as Commissioner of Mental Diseases for Massachusetts. Long-trained in the service of the State in its various hospitals, Dr. Overholser was Commissioner of Mental Diseases from 1932 to 1936. At the expiration of his term, the then governor failed to reappoint him. It is difficult to think of a man better equipped for the position. His record, moreover, was not to be questioned. Now, at least, his worth as a psychiatrist has been recognized and in going to Washington he will carry the best wishes of the medical profession.

COMMONWEALTH FUND SCHOLARSHIPS

Four first-year medical students at Tufts College Medical School are the recipients of Commonwealth Fund Scholarships. They are graduates from Harvard College, Boston College, Massachusetts State College and Duke University, respectively. Each scholarship carries a grant of $1,000 and will be renewed each year throughout the school course provided the holder makes a creditable scholastic record.

All recipients must agree to take rotating internships at approved hospitals and to practice in a rural community in Massachusetts for at least three years.

NATIONAL ADVISORY CANCER COUNCIL

The six members of the National Advisory Cancer Council, which will direct the work at the National Cancer Institute, recently established by Congress, have been announced by Dr. Thomas Parran of the United States Public Health Service. They are: Dr. James B. Conant, president of Harvard University; Dr. Clarence C. Little, managing director of the American Society for the Control of Cancer; Dr. Francis C. Wood, of Columbia University; Dr. James Ewing, of Cornell University; Dr. Ludvig Hektoen, of the University of Chicago, and Dr. Arthur H. Compton, of the University of Chicago.

CORRESPONDENCE

THE SIGNIFICANCE OF THE BIRTH CONTROL TRIALS

To the Editor: The arrest and conviction of a physician in Salem on the charge of furnishing contraceptive advice to a married woman with a systolic blood pressure of 214 millimeters of mercury was commented upon editorially in your *Journal* (August 12, 1937). Since that arrest, two Mothers' Health Offices, one in Brookline and one in Boston, as well as the headquarters of the Massachusetts Birth Control League, have been raided. The physician in charge of the Brookline office was tried in the Brookline District Court and found guilty of "exhibiting" articles used for contraceptive purposes.

During the course of the trial, Judge Parker stated that he thought it might be legal for physicians to give such advice in their private offices, but he did not believe the statute could be interpreted as allowing such advice to be given in a clinic operated for that purpose. Apparently his opinion was not influenced by the fact that the office in Brookline accepted as patients only married women whose physical or mental condition was such that pregnancy would be dangerous and that the patients who applied belonged to the class that could not afford to go to private physicians.

In the trial of the president and the educational secretary of the Birth Control League, the prosecution, according to the *Boston Herald's* report of the trial, admitted that physicians should be permitted to prescribe contraceptives for the preservation of the life and health of married women, but contended that the distribution of literature telling where such advice could be obtained was illegal. In this trial, the judge reserved his decision until October 6.

In reviewing the conduct of these trials, one is impressed by the lack of unanimity on the part of the judges regarding the interpretation of the statutes involved, and by the efforts made by the prosecuting attorneys to attribute improper motives to the physicians in charge of the offices. Both these physicians are women of the highest integrity, graduates of Tufts College Medical School, who were conducting their clinics with strict regard for the medical indications imposed by a committee of consulting physicians. The two decisions given in these cases were rendered without consideration of the fact that the right of physicians to give contraceptive advice for health reasons has the sanction of the American Medical Association and has been upheld by the United States Circuit Court of Appeals.

The seizure of the records and case histories of the Salem Mothers' Health Office was a violation of privileged communications; when a similar police action took place in New York City, there were instant resolutions of protest from the New York County Medical Society and the New York Academy of Medicine.

I cannot believe that the people of Massachusetts do in fact wish to deny to married women whose condition of health contraindicates pregnancy, but whose poverty prevents them from employing a private physician, that knowledge of contraceptive methods which is available to women in better financial circumstances. I cannot believe that it was the intention of the legislators who put

these statutes upon the books to interfere with the right of physicians to give advice which will conserve the health of their patients. I do believe that it is contrary to the principles upon which our civilization is based to make legally accessible to the well-to-do that which the law denies to the poor.

GEORGE G. SMITH, M.D.

6 Commonwealth Avenue,
Boston.

SEROLOGIC TESTS FOR SYPHILIS

To the Editor: The United States Public Health Service has been interested in evaluating the accuracy of serologic tests for syphilis done by state laboratories. This study has shown considerable variation in the reports on the same specimens of blood as to sensitivity and specificity.

This department will undertake a similar survey of hospital and public laboratories in Massachusetts for the ultimate purpose of securing uniformity of procedures. I am enclosing a copy of a letter in regard to this plan.

HENRY D. CHADWICK, M.D.,
Commissioner of Public Health.

State House, Boston.

* * *

Recent nation-wide surveys of state and other laboratories have disclosed marked differences in the efficiency of their serologic tests for syphilis. This has led the Surgeon General of the U. S. Public Health Service to recommend that state laboratories conduct similar comparative tests for the private, hospital and city laboratories in their own states. In this way the individual laboratories will gain information of the sensitivity (accuracy in detection of syphilis) and specificity (freedom from false positives) of the method they are using in relation to the methods employed in other laboratories within the state. The Massachusetts Department of Public Health will undertake one or more such surveys this fall and winter and will furnish approximately 200 syphilitic and 100 presumably nonsyphilitic specimens of blood to participating laboratories.

Although it is planned to publish the results of these surveys, the participating laboratories will be identified by number, not by name.

The directors of private, hospital and city laboratories interested in this evaluation of their serologic tests for syphilis are invited to communicate with Dr. W. A. Hinton, Wassermann Laboratory, 25 Shattuck Street, Boston.

RECENT DEATH

JONES — FREDERICK ELLIS JONES, M.D., of Hancock Street, Quincy, died September 29, at the Quincy City Hospital. He was in his sixty-fifth year.

Born in Quincy, he attended the public schools there, and entered Harvard University, graduating in 1897 from Harvard Medical School. He then started practice and served as chief surgeon for the Bethlehem Shipbuilding Corporation until his recent resignation.

A former Quincy health commissioner, he served for more than forty years as medical examiner of the eastern section of Norfolk County. Dr. Jones was a lieutenant colonel in the Yankee Division during the War, and also a veteran of the Mexican border war.

He was a fellow of the Massachusetts Medical Society, having served as a member of the Committee on State and National Legislation, and was a member of the American Medical Association.

His memberships included the Harvard Medical Society, the Neighborhood Club, the Masons and the Harvard Club of Quincy. He was a staff member of the Norfolk County and the Quincy City hospitals; past commander of the Quincy Post, American Legion; president of the Quincy Column Turning Company, a granite concern; fleet doctor of the Quincy Yacht Club; and president of the Wollaston Golf Club.

His widow, three daughters, two brothers and eight grandchildren survive him.

NOTICES

ANNOUNCEMENT

SAMUEL H. EPSTEIN, M.D., announces his return to practice in Boston, with an office in the Lister Building, 475 Commonwealth Avenue. Telephone: Kenmore 2050.

REMOVAL

G. KENNETH COONSE, M.D., announces the removal of his office to 270 Commonwealth Avenue, Boston. Telephone: Kenmore 8100.

BOSTON CITY HOSPITAL

CONFERENCE ON CLINICAL PATHOLOGY

A monthly conference on clinical pathology will be held at the hospital on Wednesday, October 13, at 12 o'clock noon, in the Pathological Amphitheater.

JOSEPH E. HALLISEY, M.D.,
Secretary, Medical Staff.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next examinations (written and review of case histories) for Group B candidates will be held in various cities of the United States and Canada on Saturday, November 6, 1937, and Saturday, February 5, 1938. Application for admission to these examinations must be filed on an official application form in the office of the secretary at least sixty days prior to these dates.

The general oral, clinical and pathological examinations for all candidates (Groups A and B) will be conducted by the entire board, meeting in San Francisco, California, on June 13, and 14, 1938, immediately prior to the meeting of the American Medical Association.

Application for admission to Group A examinations must be on file in the secretary's office before April 1, 1938.

For further information and application blanks address Dr. Paul Titus, *Secretary,* 1015 Highland Building, Pittsburgh (6), Pa.

SOUTH END MEDICAL CLUB

The opening meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, October 19, at 12 noon.

The speaker will be Soma Weiss, M.D., associate professor of medicine, Harvard Medical School; director, Second and Fourth Medical Services (Harvard), Boston City Hospital. His subject will be "Syncope, Collapse and Shock."

All physicians are cordially invited to attend. The usual luncheon will be served.

JOHN B. HALL, M.D., *Secretary.*

MASSACHUSETTS GENERAL HOSPITAL MEETING

Dr. Andrew Conway Ivy, Nathan Smith Davis Professor of Physiology and of Pharmacology, Northwestern University Medical School, will speak in the Ether Dome, Massachusetts General Hospital, at 12 noon, Friday, October 8, on "Oral Enzyme Therapy and Bile Formation."

Physicians are cordially invited.

NORFOLK DISTRICT MEDICAL SOCIETY

A stated meeting of the society will be held in the amphitheater of the Beth Israel Hospital, Tuesday evening, October 26, at 8:15 p. m.

Dr. William Dameshek will speak on "Leukemia and Related Disorders."

Discussion and a collation will follow.

F. S. CRUICKSHANK, M.D., *Secretary.*

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, OCTOBER 11

WEDNESDAY, OCTOBER 13

*9 a. m. - 10 a. m. Boston Dispensary. Hospital Case Presentation. Dr. S. J. Thannhauser.

*12 m. Clinicopathological conference. Children's Hospital Amphitheater.

12 m. Boston City Hospital, Conference on Clinical Pathology. Pathological Amphitheater.

2 p. m. Massachusetts General Hospital. Psychiatric Clinic, Outpatient Department.

THURSDAY, OCTOBER 14

9 a. m. Massachusetts General Hospital. Surgical Grand Rounds.

*9 a. m. - 10 a. m. Boston Dispensary. The Menopausal Syndrome and Its Treatment. Dr. Charles W. Lawrence.

9:15 a. m. Massachusetts General Hospital. Neurological Conference, Ether Dome.

12 m. Massachusetts General Hospital. Clinicopathological Conference.

FRIDAY, OCTOBER 15

*9 a. m. - 10 a. m. Boston Dispensary. Artificial Fever. Dr. Harry C. Solomon.

10 a. m. Massachusetts General Hospital. Fracture Rounds.

12 m. Massachusetts General Hospital. Clinical meeting of the staff of the Children's Medical Service. Ether Dome.

SATURDAY, OCTOBER 16

*9 a. m. - 10 a. m. Boston Dispensary. Hospital Case Presentation. Dr. S. J. Thannhauser.

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

*Open to the medical profession.

OCTOBER 7—Faulkner Hospital Clinicopathological Conference. 5 p. m.

OCTOBER 8—Massachusetts General Hospital meeting. Notice above.

OCTOBER 9—Boston City Hospital, staff clinical meeting, Cheever Amphitheater, 10 a. m.

OCTOBER 9—American Board of Ophthalmology, Chicago. Page 722, issue of April 22.

OCTOBER 13—Boston City Hospital, Conference on Clinical Pathology. Page 609.

OCTOBER 14—Pentucket Association of Physicians. Hotel Bartlett, 95 Main Street, Haverhill, 8:30 p. m.

OCTOBER 14-16—Association of Military Surgeons of the United States. Page 379, issue of August 26.

OCTOBER 18-22—Interstate Postgraduate Medical Association. Page 418, issue of September 2.

OCTOBER 19—South End Medical Club. Page 609.

OCTOBER 19, 20 and 21—Academy of Physical Medicine. Page 723, issue of April 22, and page 288, issue of August 12.

OCTOBER 25-29—American College of Surgeons. Chicago, Illinois.

NOVEMBER 1-12—1937 Graduate Fortnight of the New York Academy of Medicine. Page 1000, issue of June 3.

NOVEMBER 6—American Board of Obstetrics and Gynecology. Page 153, issue of July 22, and page 609. FEBRUARY 5—Page 609. JUNE 13 and 14—Page 153, issue of July 22 and page 609.

APRIL 4-8, 1938—The American College of Physicians. Page 41, issue of July 1.

DISTRICT MEDICAL SOCIETIES

BRISTOL SOUTH

NOVEMBER 4—5 p. m., Fall River.

MAY 5, 1938—5 p. m., New Bedford.

ESSEX NORTH

NOVEMBER 4—Censors' meeting, 4 p. m. Hotel Bartlett, Haverhill.

FRANKLIN

Meetings will be held at the Franklin County Hospital, Greenfield, at 11 a. m. the second Tuesdays of November, January, March and May.

HAMPDEN

Meetings will be held on the third Thursdays in October, January, April and July.

MIDDLESEX EAST

Meetings will be held at the Bear Hill Golf Club, Stoneham, at 12:15 p. m. on October 13, November 17, January 12, March 16, and May 11.

MIDDLESEX NORTH

Meetings will be held at the Vesper Country Club, Lowell, on October 27, January 26, and April 27.

NORFOLK DISTRICT

OCTOBER 26—Notice above.

NORFOLK SOUTH

OCTOBER 7—Norfolk County Hospital, South Braintree, 12 noon.

PLYMOUTH

Meetings will be held at 11 a. m. on October 21, November 18, January 20, March 17, April 21, May 19 and July 21.

SUFFOLK

OCTOBER 25—Joint meeting with New England Heart Association. (Program and speakers to be announced.)

NOVEMBER 17—Joint meeting with Boston Orthopedic Society.

JANUARY 19—Joint meeting with Boston Medical Library.

MARCH 15—Joint meeting with Boston Obstetrical Society.

WORCESTER

At the following meetings, except the annual meeting, dinner will be at 6:15, to be followed by business session and scientific program.

OCTOBER 13—Rutland State Sanatorium, Rutland.

NOVEMBER 10—Grafton State Hospital, North Grafton.

DECEMBER 8—St. Vincent Hospital, Worcester.

JANUARY 12—Worcester City Hospital, Worcester.

FEBRUARY 9—Worcester State Hospital, Worcester.

MARCH 9—Memorial Hospital, Worcester.

APRIL 13—Hahnemann Hospital, Worcester.

MAY 11—Afternoon and evening, annual meeting. Place and schedule of program to be announced.

WORCESTER NORTH

OCTOBER 20—State Colony, Gardner, 4 p. m. Details to be announced.

BOOKS RECEIVED FOR REVIEW

General Hygiene and Preventive Medicine: A text-book for college students, medical students, nurses, public health workers and social workers. John Weinzirl. Edited by Adolph Weinzirl. 424 pp. Philadelphia: Lea & Febiger, 1937. $4.00.

The Rockefeller Foundation. Annual report, 1936. 461 pp. New York: Rockefeller Foundation, 1937.

Maternal Deaths: The ways to prevention. Iago Galdston. 115 pp. New York: The Commonwealth Fund, 1937. Clothbound, 75c; paperbound 50c.

The Therapeutic Problem in Bowel Obstructions: A physiological and clinical consideration. Owen H. Wangensteen. 360 pp. Springfield and Baltimore: Charles C Thomas, 1937. $6.00.